

Black Arrow Aborts

THE only complaint to make about the abandonment of the development of the Black Arrow rocket (see page 362) is that the decision was not taken several years ago. Since 1964, when the programme was begun, only a few enthusiasts have professed conviction that they knew what Black Arrow might accomplish. To most people, it has been clear all along that the fully developed rocket would be too small to accomplish the tasks which the then government specified for it. The result is that more than £11 million has been for practical purposes wasted on the development programme and on the launching of three rockets at a cost of £2 million each. The question whether the programme should continue has no doubt been brought to a head by the failure last year of an attempt to attain an Earth orbit. In the circumstances, there will clearly be a great many pairs of crossed fingers as the time approaches, later this year, for the attempt to launch the X3 satellite. Whatever happens, however, that will be the last monument to Black Arrow. Thereafter, the British Government will turn, as it might have done in the first place, to the National Aeronautics and Space Administration in the United States. It is earnestly to be hoped that the talk now to be heard of rekindled British interest in a European launcher rocket is, for the time being at least, all smoke and no fire. In the meantime, three questions should be answered—what can be done to prevent similar mistakes in the years ahead, what strategy should be adopted for the development of space research in Britain and what opportunities are there, in this hard-headed world, for making money out of space?

Black Arrow was born of compromise. Quite sensibly, after the unhappy experiences of the early sixties, with the concept of a military rocket able to carry nuclear warheads from one place to another, the British Government was persuaded that it could not set up in business as an independent satellite launcher. That, in any case, was what the European Launcher Development Organization (ELDO) was meant to accomplish but there was a seductive line of argument that there would be serious dangers in contracting out of what was called space technology—the design and operation of solar cells, ion rockets and the like. The result was the decision to develop a launch vehicle capable of putting experimental packages into orbit but not big enough to launch satellites of any practical value in applications. (The scheme for using electrical propulsion driven by solar cells as a means of progressively driving out the orbit of such a satellite to geostationary distances is ingenious enough but unlikely to compete successfully with techniques of satellite launching that achieve a geostationary orbit at one fell swoop.) Worse still, however, the Black Arrow development programme was run on a shoestring. For the first year and a half, until the beginning of 1966, contracts were awarded for periods of three months at a time, with the result that those working on the programme were frustrated and, predictably, by the time Black Arrow was in service, most of what it might have achieved had already been done elsewhere. It is also now a familiar experience, in several other countries as well as the United Kingdom, that

it is not safe to base a rocket development project on a single launching once a year. The waste of time and money if one rocket should fail (as one and a half have done with Black Arrow) cancels out the economies that parsimony brings. This is the point which the Estimates Committee of the House of Commons singled out for special complaint in 1967, but nothing much has been done since then to put the programme on a better footing. The moral, of course is that there is no point in trying to enter a quickly growing branch of advanced technology with only just enough resources to wet the feet. Black Arrow has been an unnecessary but expensive product of wishful thinking.

What should happen next? Plainly the British Government cannot hope to mount programmes comparable in scale even with the malnourished Black Arrow programme without spending much larger sums of money than it is accustomed to devote to work like this. In the past five years, the Black Arrow programme has accounted for more than one-sixth of expenditure on space research and technology carried out by British organizations. At the moment, Black Arrow is running at about twenty per cent of this same expenditure. Evidently it would be quite out of the question to mount a more effective programme to succeed Black Arrow without increasing the space budget by several million pounds a year and by recognizing that close on a half of all national expenditure on space research and technology would go on this new venture. That, evidently, is out of the question. In any case, the defence research programme, which has already led to the valuable Skynet communications satellite, is probably a sufficient guarantee that British laboratories will know what the Joneses are doing even if they cannot keep up with them in every respect. In the circumstances, British policy should aim at making sure that at least some British organizations will be able to make effective bids for the Intelsat contract that should then become available for building communications satellites. Nobody should be ashamed of asking NASA to keep on launching scientific satellites labelled with a Union Jack. What matters there, as every scientist will say, is whether the satellites are launched successfully and whether they function well when once in orbit.

But is there money to be made? It is perhaps salutary to recall that communications satellites are potentially valuable because they are, above all, cheap. The first five copies of the Intelsat IV satellite, each with up to 6,000 telephone circuits or their equivalent, cost Intelsat \$72 million and it seems to be acknowledged that the price would have been lower if Comsat had been a better manager. The second five copies cost less than half as much, and are likely to satisfy the needs of Intelsat for the rest of this decade. The questions that governments like the British should ask themselves is how much it may be worth spending to win a chance of competing successfully for a business that seems to amount to something of the order of \$100 million a decade, or \$10 to \$20 million a year. On the face of things, it would be safer to put the money into a programme for developing



a technology in some more reliable market, typewriters for example. To be sure, the enthusiasts such as the British Aircraft Corporation say that in due course there will be a rich market for supplying communications satellites to individual countries or groups of countries wishing to have one to themselves, or even in broadcasting educational television. The trouble here is that the market may not exist at all—much depends on the outcome of experiments still to be mounted as well as on the regulations adopted by governments to control the importation of television programmes from outside. And

applications of communications satellites other than in telecommunications, socially valuable though they may be, are necessarily less prolific markets for the satellite builders. From a strictly national point of view, in other words, as well as from all others, it is essential that the British Government, now embarked on yet another review of "the national space technology programme", should try to head off the enthusiasm of the country's aerospace industry as it calls itself, and that it should persuade them to put their backs into more mundane activities such as telephone switching equipment.

Sheep and Goats

GOVERNMENTS on both sides of the Atlantic have in the past week been perplexed by the need to make decisions about the future of important enterprises. In the United States, the Senate on Monday this week did finally agree, over Mr William Proxmire's protesting but much alive body, to provide a guarantee for a bank loan to the Lockheed Company so as to provide it with the finance necessary to keep the company alive. In Britain, the government has taken a similar view about its attitude towards the computer company International Computers Limited, which in the past few months has from time to time been alarmed by harsh words from government ministers anxious to impress on all kinds of industries that nothing stands between a company and bankruptcy except profit. Although no money will change hands in an obvious sense, ICL will be helped along by government research contracts and will also benefit from a procurement policy likely in the future to be more effective than in the past (see page 360). Other computer companies in Britain are understandably upset by this development, especially because many of them must have been calculating that the impending entry of Britain into the EEC would have been a splendid way of extending their influence on the mainland.

In case the British Government should be considered to be backsliding from the spartan views which Mr John Davies at the Department of Trade and Industry has been advocating in the past year, however, no less a person than Mr Davies himself stood up in the House of Commons last Friday to pronounce the end of government support for Upper Clyde Shipbuilders Limited, an amalgamation of four Scottish shipbuilding yards which has been supported since 1967 with a total of £27 million and which is now in bankruptcy. No doubt this decision would have been an even more dramatic incident if the workers affected had meekly joined the dole queue; instead they have quixotically kept on working. But for them and taxpayers everywhere, it may be important to know by what criteria conservative governments in the United States and Britain have decided to go against their principles and prop up lame ducks. Why is Upper Clyde Shipbuilders less deserving than International Computers Limited?

The most obvious difference is that shipbuilding is, so far as Britain is concerned, an ageing industry, while International Computers Limited is at least an enterprise that may bring profit in the years ahead. In other words, it may well seem that what the British Government is doing is prudently to invest in the future and sensibly to wash its hands of the past. The difficulty, of course, is

that industrial issues are never as simple as this. Ever since the publication of the Geddes report on shipbuilding five years ago, it has been clear that there is nothing wrong with British shipbuilding except the way in which the industry is organized. There have been too many yards, too many builders of marine engines, too little equipment which is modern and efficient and too casual a sense of the difference between profitability and failure.

Upper Clyde Shipbuilders came into being partly because of the then government's wish to make progress along the lines suggested by the Geddes Commission and partly because of its wish to encourage some novel, almost syndicalist, experiments in labour relations at the Fairfield's yard, one of those now amalgamated into Upper Clyde Shipbuilders. Perhaps, in retrospect, nobody should be surprised that the prospect of closure has stimulated schemes for enabling workers to assume and retain control. Yet the case of British shipbuilding is entirely similar to that of British textiles two decades earlier—too many companies, too little productivity insufficiently compensated for by low wages, too little new machinery and no semblance of financial understanding, let alone control. The Geddes Commission in 1967 would have done well to have spelt this out more clearly. The last government would have done the shipyards as well as its reputation a service by looking for radical solutions to shipbuilders' problems, not by attempting to paper over the cracks with what is now acknowledged to be a theoretical merger.

As things have turned out, the steps that might have been painless four years ago have now been forced on the shipyards, on the government and on the people of Clydeside. In his first statement, last week, Mr John Davies spoke as if the issue was simply a question of cash, and there is of course no doubt that in strictly commercial terms, Upper Clyde Shipbuilders are bankrupt. Even if they were able to finish off their ships on time, they would be almost certain to lose money on them. No doubt the independent (but some say biased) committee which provided the government with advice is right to have said that work would have to be concentrated on two yards, not four, and it is logical for the government to take the line that even such a solution will be acceptable only if private industry seems inclined to take a risk in building ships on the Upper Clyde. Yet is it proper for a government to wash its hands as easily as Mr Davies has done of responsibilities implicitly incurred by its predecessor? Rightly or wrongly, most probably wrongly. Mr Anthony Wedgwood Benn, when Minister of Technology, allowed public funds to be engaged in keeping the Upper Clyde Shipbuilders going from one crisis to

the next. By doing so, he helped to create an illusion of security among the 9,000 people on the payroll. Is it permissible now for his successor to pretend that such an implicit commitment can be dismissed simply because the government has changed? It is creditable that Mr Davies's contribution to the debate in the House of Commons last Monday did more to acknowledge that it is unseemly to throw 4,000 people out of work in an area in which unemployment is already high. It is a question whether, in circumstances like these, the government does not owe the community a much more active campaign to help ensure that the consequences of shutdown are ameliorated. This, after all, is one of the continuing roles of governments in advanced societies in which old industries must continually be overtaken by new.

A second complaint against what may be a perfectly respectable decision to recognize the bankruptcy of Upper Clyde Shipbuilders Limited is that the government has in its present way of thinking no means of encouraging the kind of rationalization of the shipbuilding industry which needs to be attempted. It is all very well to say that governments should let industries and companies demonstrate by performance whether they can sink or swim but this is too passive a point of view. There are, after all, carrots as well as sticks, and it should not be beyond the wit of governments such as even the present to devise ways of moulding the shipbuilding industry in Britain into a pattern which is commonly held to be viable. To be sure, there are some theoretical difficulties in the way for those who believe that only the natural tug of war to which industrial companies are naturally exposed can be relied upon to chart the course for the years ahead, but this is like saying (as some heuristically inclined educationists insist) that if you put a child in an empty room and leave him for long enough, he will rediscover Newton's laws. The truth is that there are plenty of ways of combining carrots with sticks so as to catalyse the process of self-discovery. What the shipbuilding industry in Britain needs is more encouragement to invest in new equipment and more vigorous criticism of its performance. The government would do a public service if it recognized that it must play a part in bringing out these conflicting pressures in the industry. After all, there are several candidates in line for similar treatment. After shipbuilding will come the motor car industry. Can machine tools be far behind?

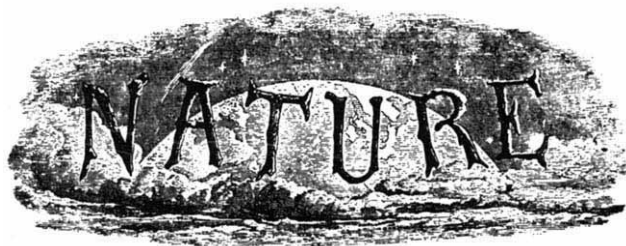
By these standards, the plan to give ICL a sense of security which it has not entirely earned by its own efforts leaves much to be desired. The chief difficulty is that there is no means of knowing whether it is possible to organize a computer company on a strictly national basis. With shipbuilding, it is true, comparatively small enterprises can succeed—the Scandinavians and the Japanese have shown precisely that. But with computer manufacturers, the high cost of meaningful research and development puts computer manufacturing in a class with aircraft manufacture and petroleum production. The chances are that the most straightforward way of launching such an enterprise is to have access to several markets and to several sources of technical skill. It may be the case that the British Government is building up ICL as a kind of dowry with which to join the EEC. It is also of course true that ICL itself has been enterprising in forging links with companies abroad, notably the Control Data Corporation (but its association with RCA has come to an end in the past few weeks). In all the circumstances, there

is a danger that the British Government may be seeking to prop up an organization in the wrong pattern. This is the error which its predecessors made, but it may be a little more demeaning that the mistake on this occasion resembles that by means of which tiny governments give themselves an air of going places by sponsoring with taxpayers' money airlines which cannot be commercially viable.

The case of Lockheed is very similar. Ironically, the Senate's narrow endorsement by one vote of the earlier decision by the House of Representatives to guarantee a loan of \$250 million to a corporation already in the red to the tune of \$400 million came just a week after the first flight of the Douglas DC-10, an aircraft that would be entirely competitive with the Lockheed Tri-Star airbus if the two manufacturers had not insisted in advance that potential customers should place firm orders and make appropriate non-returnable deposits as marks of their good faith. As it happens, the putative customers now regret having placed their orders, for air traffic has lagged behind the forecasts of a few years ago. The ideal outcome of the trouble about Lockheed would have been a merger with Douglas, even though that might well have left the luckless Rolls-Royce with nothing to keep the RB211 engine alive.

What Congress has now done is to help support an entirely laudable organization which is nevertheless cast in the wrong mould—in spite of the buoyancy and the commercial resilience of the American based airlines, the United States is already too small to support three large suppliers of civil aircraft. As with computers, so with aircraft, the development costs are necessarily so high that only multinational companies can hope to be successful. But Lockheed is, like its competitors, also closely tied to national programmes for defence research and development. Congress would have done better for Lockheed, for airlines and for American taxpayers if it had found some way of pushing the company towards a different strategy for organization with less dependence on the domestic market and the local government. Like the British shipbuilders and the British computer manufacturers, American aircraft manufacturers are in danger of strangling themselves with too little imagination. There are no sheep, they are all goats.

100 Years Ago



THE charge against Mr. Hampden of libelling Mr. Wallace was tried on Thursday week in the Secondary's Court. Our readers will remember that a wager of 500*l.* having been made between Mr. Hampden, who affirmed that the world was flat and not round, and Mr. Wallace, it was decided against the former, who thereupon abused Mr. Wallace as a liar and a swindler. The action now tried was for damages for these and other similar libels, and Mr. Hampden was condemned to pay 600*l.* damages.

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OLD WORLD

GAS CENTRIFUGE

All Set for Bensberg

EUROPEAN uranium enrichers in Britain, Germany and Holland are now able to point to at least one tangible sign of progress—the formal establishment of the German-based company called CENTEC at Bensberg, near Cologne, on July 29. The new company, formally known as CENTEC Gesellschaft für Centrifugentechnik mbH, will be responsible for the research and development programme which, the sponsors hope, will yield a couple of functioning pilot plants by about 1975, one in Britain and one in Holland. When the technical and economic feasibility of gas centrifuge machines for enriching uranium has been assessed, CENTEC will be empowered to design and build enrichment plants to the orders of its customers. As at present foreseen, the principal customer will be a company called URENCO, similarly sponsored by the three governments of Britain, Germany and Holland, which will be able to process and to sell enriched uranium to potential users. Theoretically, CENTEC will also be able to sell enrichment plants to countries not involved in the development programme, but obviously the sponsoring governments will be more anxious to set up as successful suppliers of enriched uranium, with the continuing profit that that will bring, than to supply outside parties with opportunities to set up in competition. URENCO has not yet been formally established, but its shareholders will be, as with CENTEC, the Dutch company Ultra-Centrifuge Nederland NV, the German company Gesellschaft für Nukleare Verfahrenstechnik mbH and British Nuclear Fuels Limited.

Those involved with the new development seem to be as optimistic now as were the three sponsoring governments when news of the possible use of gas centrifuges in uranium enrichment was first made public two years ago. By all accounts, individual centrifuge machines have been tried out separately and in cascade, with the result that the designers are confident that the machines will function. The questions to be decided chiefly concern the cost of production. Mr T. Tuohy, managing director of British Nuclear Fuels Limited and a director of CENTEC, said earlier this week that the obvious target at which to aim is the United States Atomic Energy Commission price of \$32 per ton of separated work, the equivalent of \$35 per ton delivered in Europe. He said that he and his colleagues were optimistic about the prospects—that this goal could be attained.

The chairman of the board of the new

German-based company is Dr Ir Han Hoog, recently retired as a director of Shell Petroleum Limited and its Dutch equivalent. The general manager of the new company is Mr David Peirson, secretary of the UK Atomic Energy Authority for the past sixteen years. The new company's budget is not publicly available, although it is expected that total development costs will be several million pounds. Under the arrangements which have been worked out so far, research contracts will be farmed out by CENTEC to the three shareholding companies. The result is that only the technical staff of CENTEC will be in a position to make an overall assessment of the programme of research and development.

SCIENTISTS' PAY

Calm Before the Storm

BOTH sides involved in the scientists' pay dispute are, this week, taking stock of the situation before the official arbitration tribunal sits next Thursday, August 12. The Institution of Professional Civil Servants (IPCS) has organized a public meeting scheduled for 7.00 p.m. on August 10 at the Central Hall, Westminster, to bring to a climax its campaign that started at Abingdon three weeks ago.

These meetings have attracted large numbers of people but they have produced no visible change in the attitude of the Civil Service Department. A spokesman for the department said earlier this week that he could not comment on the strength of feeling shown at the IPCS meetings, but that the official side's case—based on the findings of the Pay Research Unit—had already been submitted to the tribunal. The unit's report has been interpreted by the government to show that a scientist within the Scientific Civil Service is as well off financially as his counterpart in industry.

The institution counters this by saying that the comparison is unfair in the sense that several of the companies included in the pay research exercise base their salaries on what the government pays scientists. It also says that the government's offer makes no allowance for the fact that the administrative grades within the Civil Service received a pay award earlier this year and so this present offer destroys the concept of internal relativity within the Civil Service.

Mr William McCall, the general secretary of the IPCS, said earlier this week that any independent body would be certain to recognize the merits of the institution's case and that he was confident that the outcome of the tribunal would be favourable to the scientists. Mr McCall also said that

if the tribunal does not produce what he expects, he will press for a review of the basis for determining scientists' salaries within the Civil Service.

Whatever the findings of the tribunal, there will be pressure to change the procedure used to determine government scientists' salaries. If there is no award, the IPCS will evidently seek to change the system. If, on the other hand, the tribunal recommends all or even part of the claim, then the whole of the pay research investigation will be invalidated. For outsiders, however, it remains a paradox that the report of this Pay Research Unit is still confidential between the Civil Service Department and the IPCS.

The question of whether the report of the Pay Research Unit should be made public was raised in the House of Commons on July 29 when the Prime Minister, Mr Edward Heath, told Mr Tam Dalyell that the decision to abide by the recommendations of the Pay Research Unit was originally made by the previous government, but that "it does not seem justifiable, when the pay is above those already working outside, that those concerned should still have increases of salary". The Prime Minister added that he would enquire into the possibility of making public the report of the Pay Research Unit.

COMPUTERS

No Breadline for ICL

THE announcement last week by Mr Frederick Corfield, Minister for Aerospace, that the British Government would continue to support International Computers Limited is certainly a shot in the arm for the company, but the decision has aroused some strong feelings among the other computer companies in Britain. These, mostly offshoots of United States corporations, naturally feel hard done by and their strongest complaint is that the minister has apparently reversed previous government policy in granting further research and development money to ICL.

ICL has always been in a privileged position in the supply of computers to government departments, and the new statement will ensure that it remains so. The company's position is determined by single tender orders which involve no competition from other manufacturers. Such preferential treatment should ensure a thriving company, but the signs are that all is not well at ICL, with 1,800 redundancies announced last week to add to the 1,600 announced earlier this year. Sir John Wall, the chairman of ICL, has said, however, that the company is in good shape and that the pessimism about the future is not well founded. Sir John also stated that the

cut back in staff was evidence of ICL's determination to live within its resources.

International Business Machines Limited has been maintaining a dignified silence about the events of the past few days, but the Honeywell company has spoken out against the government's action. Mr Donald Brosnan, chairman and managing director of Honeywell, said this week that "the policy works against the British computer industry as a whole and in particular against the development of computing in the public sector. Not only does it stifle competition but it also limits access to international technology".

The question that remains unanswered is whether the confidence placed in ICL is well founded. Are the performance and cost of ICL computers comparable to or better than their competitors? Such a comparison is not possible without a detailed analysis of the needs of a particular user; in particular it depends on the scientific/commercial balance that the computer user needs to achieve.

The computer companies stress that they will only quote performance figures for a particular job assignment. Despite this, however, it is apparent that the Honeywell 6000 series, the IBM 370 series and the ICL 1900 series are comparable and competitive.

With ICL receiving such support from the government and also in view of the pressure that is being exerted on industry and public sector bodies in Britain to buy ICL computers, it is not difficult to understand why the other companies are annoyed. Mr Brosnan expressed the feelings of these companies when he stated that Mr Corfield's statement "ignores the interest of foreign owned companies which manufacture and employ significant numbers of people in the United Kingdom (Honeywell employs 8,000). In so doing it conflicts with other stated government policies of attracting overseas investment to the nation's development areas".

EARTHQUAKE RESEARCH

What Future for Tokyo?

from a Correspondent

THERE is great anxiety among seismologists about the future of the International Institute of Seismology and Earthquake Engineering, set up in Tokyo in 1962 and supported jointly by the Japanese Government and the United Nations Development Programme. The immediate problem is to know how the institute can continue after August 1972, when the present agreement runs out. At what seems to have been a sombre meeting of the senior consultants of the institute

in Tokyo in March this year, it was accepted that continuing support for the institute would have to come from the government of Japan and from UNESCO.

The institute has a permanent staff of about twenty provided by the government of Japan. UNESCO also provides two or three "experts" each year, usually seismologists and earthquake engineers from outside Japan. The institute conducts regular lecture and laboratory courses, as do the visiting lecturers.

An average of some twenty students a year have been trained at the institute. Over the years, they have come from more than forty countries, including developing countries in Asia, Africa, South America and the Pacific region. Stipends have been provided by the government of Japan and through the UNDP Special Fund.

During 1963-68, the institute concentrated on routine training. The programme has now been extended to include an advanced course in which the emphasis is on research training. The students, some five a year, have

previously been PhD graduates or hold equivalent qualifications. The advanced students assist in the lecturing programme.

The institute has a special role in fostering seismology and earthquake engineering in developing countries, where there is an urgent need both to mitigate the effects of earthquake disasters and to fill conspicuous gaps in the global recording of earthquakes.

ASTRONOMY

South African Debate

EMOTIONS are still running high at the closing of the only strictly South African observatory, the Republic Observatory at Johannesburg. There have been bitter exchanges in the correspondence columns of *Monthly Notes of the Astronomical Society of South Africa*. The British Science Research Council is involved to the extent that the rationalization of South African astronomy was stimulated by the review of astronomy in the southern hemisphere completed late in 1968 by

Freshwater Biology

THIS is a fluvarium which was opened on July 23, together with other extensions, at the site of the River Laboratory of the Freshwater Biological Association in East Stoke, Dorset. The fluvarium, which was opened by Mr Peter Walker, Secretary of State for the Environment, has been so called because it is an aquarium in which the tanks contain flowing water. Built where once a corn mill stood, the building is a water-tight concrete box, 30 feet by 12 feet, sunk 9 feet into the ground. The roof is made of glass, and the flow of water through the fluvarium is maintained by gravity, without recourse to pumps.



a committee of four set up by the council.

Like the more recent review of astronomy in the northern hemisphere (see *Nature*, 232, 289; 1971) the report of the southern hemisphere review committee was never published. But it is understood that the committee was particularly concerned with the reduction of British commitments in South Africa with the building of the Anglo-Australia 150-inch telescope.

As a part of this plan, the Royal Observatory at the Cape of Good Hope, which has been in the hands of the Science Research Council since 1965, is to be run as a joint venture with the South African Council for Scientific and Industrial Research. At the end of this year, the Royal Observatory at the Cape will become the headquarters of what is to be known as the South African Astronomical Observatory, having as its first director Sir Richard Woolley who retires as Astronomer Royal at the end of the year. The chief facilities of the observatory, however, will not be at Cape Town, where of course city lights have long been a problem, but at a new site which is being established 235 miles to the north-east at Sutherland.

It is understood that the British contribution will be of the order of R1 million over ten years, compared with R2 million from the CSIR over the same period, and that the CSIR will have the controlling interest.

What some astronomers in South Africa and elsewhere are objecting to is that the rationalization of South African astronomy also involves the closing by the CSIR of the observatory at Johannesburg. The most vociferous support for keeping the Republic Observatory comes from Dr W. S. Finsen, who was director from 1956 (when the observatory was known as the Union Observatory) to 1965, and Dr W. H. van den Bos, director from 1941 to 1956. But Drs Finsen and van den Bos are being encouraged in their campaign by astronomers outside South Africa. Among others, Drs A. F. Cook and B. G. Marsden of the Smithsonian Astrophysical Observatory have expressed their concern about the future of long-term programmes on the positions of asteroids and on double stars at present being carried out by the Republic Observatory.

The reaction of the CSIR is that omelettes cannot be made without breaking eggs. Unfortunately, however, the continuing debate between the opposing factions is being conducted at an acrimonious and personal level, in *Monthly Notes* as well as in the Johannesburg newspapers.

Among the concerns of Drs van den Bos and Finsen seem to be that the new arrangements will put the centre

of gravity of South African astronomy in the Cape Town area. They are suspicious that the role of the Royal Observatory at the Cape as the headquarters of the new observatory was decided before the location of the new observing site was chosen, rather than the sequence of events presented by the CSIR in which the site at Sutherland was chosen first, after which the selection of the Royal Observatory as headquarters became obvious because of its proximity. But Drs van den Bos and Finsen also dispute the choice of Sutherland because its "bleak and isolated locality" (on the western edge of the Karroo) will not be attractive to observers, because of their argument that the programmes on asteroids and double planets would not benefit from being transferred to Sutherland from Johannesburg and because of their claim that South Africa contains better sites than Sutherland.

The CSIR case has been put by Dr F. J. Hewitt, chairman of the South African National Committee on Astronomy and vice-president of the CSIR. He says that the Sutherland site was selected on its merits, that the choice of the Royal Observatory as headquarters then became logical, that the Republic Observatory is in any case run down, and that "a particularly unfortunate aspect has been the attempt to involve astronomers overseas in the campaign against these new proposals".

Particularly galling to Drs van den Bos and Finsen is that the CSIR did not appoint a new director to the Republic Observatory after Dr Finsen's retirement. Since then the observatory has been making do with an acting director, Mr J. Hers.

It is regrettable that the debate is taking place only after the decision on the South African Astronomical Observatory was announced by the CSIR on September 23 last year. As things stand, the efforts of Drs van den Bos and Finsen are in danger of being regarded as a lost cause being conducted by the old guard of South African astronomers reluctant to be moved from Johannesburg. Nevertheless, since the CSIR took over the running of the Republic Observatory from the South African Government in 1964, the CSIR has had the responsibility of seeing that rearrangements are made only after proper consultation, an obligation which Drs van den Bos and Finsen would say has not been carried out.

Meanwhile, it appears that the 26½-inch refractor at the Republic Observatory—the largest instrument and about fifty years old—is likely to continue in operation at Johannesburg for two or three years more. The observatory Franklin-Adams used for work

on asteroids and comets at a site 50 miles outside Johannesburg is expected to remain where it is for a year or two. Discussions are going on about what to do with the other aspects of the work of the observatory—chiefly the maintenance of the national time service—and the observatory's library is being moved to Cape Town.

The rationalization now planned takes no account of the Radcliffe Observatory at Pretoria, which has in the past been financed by the British Science Research Council. For some time, the council has been saying that its support will end in 1974, and the Radcliffe Trustees, the formal owners of the observatory, would be hard pressed to know where to look for continued support. But the Radcliffe Observatory has a splendid 74-inch reflector, and the plans for the Sutherland site so far include no large telescope. Is it too much of a coincidence that 1974 would be a good time to move the Radcliffe instrument from Pretoria? And is there now a danger that that would be a further thorn in the flesh of the Afrikaners on the Rand, ever suspicious of the Cape? After all, a site three-quarters of the way to the Cape does not seem like a no man's land even if it is mostly desert.

The consensus among astronomers is probably favourable towards the efforts by the CSIR to provide a strong centre for South African astronomy. In spite of several successes, astronomy in South Africa has not had the reputation that should have come to one of the few countries favourably placed to observe the relatively unexplored southern skies, which include the galactic centre and the Magellanic Clouds. The South African observatories have already been eclipsed by the observatories in Chile, where the United States and others are investing in the remarkably clear skies of the Andes.

Nevertheless, most astronomers will also wish that the CSIR had gone about its plan with more tact. And it is obviously important that some way should be found of continuing the long term programmes on the asteroids and double stars that are being carried out by the Republic Observatory.

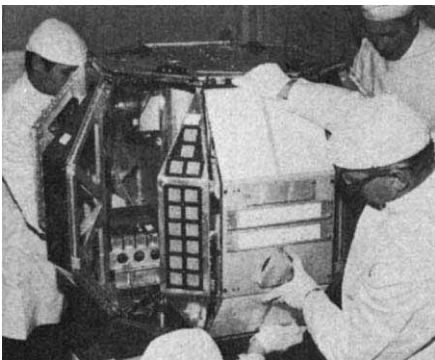
SPACE POLICY

Black Arrow Scrapped

THE British Government has decided to end the Black Arrow satellite launcher programme. This is no surprise and indeed the decision has been foreshadowed on several occasions during the past few months especially in the evidence of the Ministry of Aviation Supply and the Department of Trade and Industry before Sub-

committee B of the Select Committee on Science and Technology. It is nevertheless surprising that the government should have chosen to make its announcement only three months before the select committee is expected to publish its report and recommendations on the future of space research in Britain.

The Black Arrow rocket has been an integral part of the National Space Technology Programme for several years. Its end is a part of the review of the programme being carried out by Mr Frederick Corfield, Minister of Aerospace at the Department of Trade and Industry. The department has always argued that the programme should be oriented to achieve the best results for the smallest expenditure and with an eye on the need that British industry should gain technologically. At present, about £4.6 million a year is spent on the programme, about 20 per cent of the total for all British space activities (see Table). Of this total, about 55 per cent is spent on scientific research. The government evidently now feels that Black Arrow does not represent sufficiently good value for money. Some scientists had hoped that a British rocket would eventually be used to launch a British scientific satellite but that idea too dies with Black Arrow.

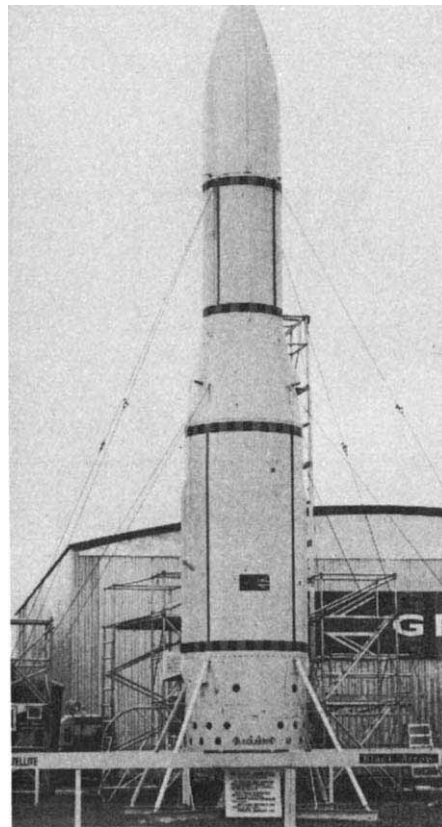


The X3 satellite due to be launched by Black Arrow in September.

The DTI seems to have convinced itself that there is very little expertise to be won from small satellites in the low level polar orbits which could be reached with Black Arrow. Nowadays, interest centres on satellites in geosta-

tionary orbits. The next launch of Black Arrow, with the X3 satellite, from Woomera during September will be the last. The planned X4 satellite will be launched from the United States on a Scout rocket.

Apart from being limited in capacity, Black Arrow is neither dependable nor cheap even allowing for the long intervals between launches, which have meant that it has never been fully tested. During the six years of development from the Black Knight rocket, £11.5 million has been spent with each launching costing £2 million. One launch has failed, one has been a success and one a partial success. The total cost of a Scout launching will be about £1.25 million. The whole rather unsatisfactory situation was summed up by the companies involved in the manufacture of the satellite who advocated earlier in evidence to Subcommittee B that Black Arrow should be fired oftener or scrapped altogether.



The Black Arrow Rocket.

The government's plans for testing much larger satellites and complete applications systems in geostationary orbit are unlikely to be spelled out before the end of the year—almost certainly after the Select Committee has presented its report. But the X4 satellite will contain a prototype system for maintaining the triaxial stability which is vital for most applications satellites, particularly for those in geostationary orbits. The Thor Delta is the obvious launcher but would cost

about £3.3 million a time.

The British Government seems to be talking as if there will be no difficulty in being able to use whichever American rockets appear best to suit its plans for launching satellites, but no formal agreement yet exists and this is a field in which private understandings are notoriously capable of being undermined by the ins and outs of governments. In the circumstances, it would not be surprising if the British Government might yet choose to collaborate in the construction of some rocket launcher within the framework of ELDO, although it is clear that many hearts would have to change before that became a painless operation.

The preliminary decisions taken last month by the council of ESRO to go ahead with a space applications programme as distinct from the scientific programme which has been ESRO's chief concern since its inception in 1962 must also have influenced the decision to scrap Black Arrow. Britain at present contributes about £5.5 million a year to ESRO (see Table) and this sum is likely to increase quite rapidly if the applications programme goes ahead smoothly. France, Germany, Italy and Britain have agreed to provide £33 million by the end of 1973 and then a minimum of £30 million a year until 1980. It must have become clear to the DTI that if British industry is to contribute in a significant way to a European applications programme and thus provide some economic feedback for the money invested in ESRO, it must gain the expertise with geostationary systems that could not be properly attained with satellites launched by Black Arrow.

The increasing involvement of the DTI with ESRO also means that the department will take on an increasing share of the representation of the UK at ESRO. At present the Department of Education and Science provides most of the representatives although it is advised by members of the Department of Trade and Industry.

One of the unresolved questions is that of British or European participation in the post-Apollo programme which still suffers from lack of definition and whose very existence seems doubtful. One of the suggestions which the United States Government made last year was that Europe should contribute "at least 10 per cent" towards the development of the post-Apollo transportation system whose total development cost would be "about £4,000 million" during the next ten years. It has been suggested, for example, that agreement to join the post-Apollo programme could pave the way for NASA to launch European applications satellites and presumably UK payloads of the same type as well.

British Space Expenditure, 1970-71 (£000 estimated)

International	
ELDO	£1,840
ESRO	£5,450
Intelsat	£1,130
Post-Apollo studies	£230
National	
Defence	£6,730
Commercial satellite communications (Post Office earth terminals)	£1,600
Scientific space research	£3,930
National Space Technology Programme	£4,640
Total	£25,550

NEW WORLD

Davis Committee Exposes the Problems

by our Washington Correspondent

THOSE who believe that the United States has a workable and explicit policy for the support of research and development had only to attend three meetings last week of the Science, Research and Development Subcommittee of the House Committee on Science and Astronautics to discover that their faith may be groundless. The subcommittee, under the chairmanship of Mr John Davis, took a speculative bite at a problem that will keep it occupied throughout the autumn and winter, but which could well require many more years of probing before worthwhile conclusions can be formed. The subject that the committee intends to study is "science, technology and the economy"; whether the committee has bitten off more than it can chew remains to be seen. Nevertheless, to judge by what the hearings uncovered last week, the subcommittee could do a valuable job in bringing even some of the more obvious problems to public attention.

Chief among the factors that will occupy the committee's attention is that the growth in expenditure on research and development in the United States has been decelerating during the past decade. During the past five years, for example, expenditure on research and development has been growing at only 0.3 per cent a year taking inflation into account, compared with a real growth rate of about 11 per cent in the late 1950s. It seems that what is most at fault is the mechanism for promoting research and development in the private sector.

What policies are needed to ensure that more funding for research and development will stimulate the flagging economy of the United States, and reverse the slide in the nation's trade balance? According to the American Federation of Labor and Congress of Industrial Organizations (AFL-CIO), the answer may be found in simply imposing federal restrictions on the outflow of capital and technology from the United States.

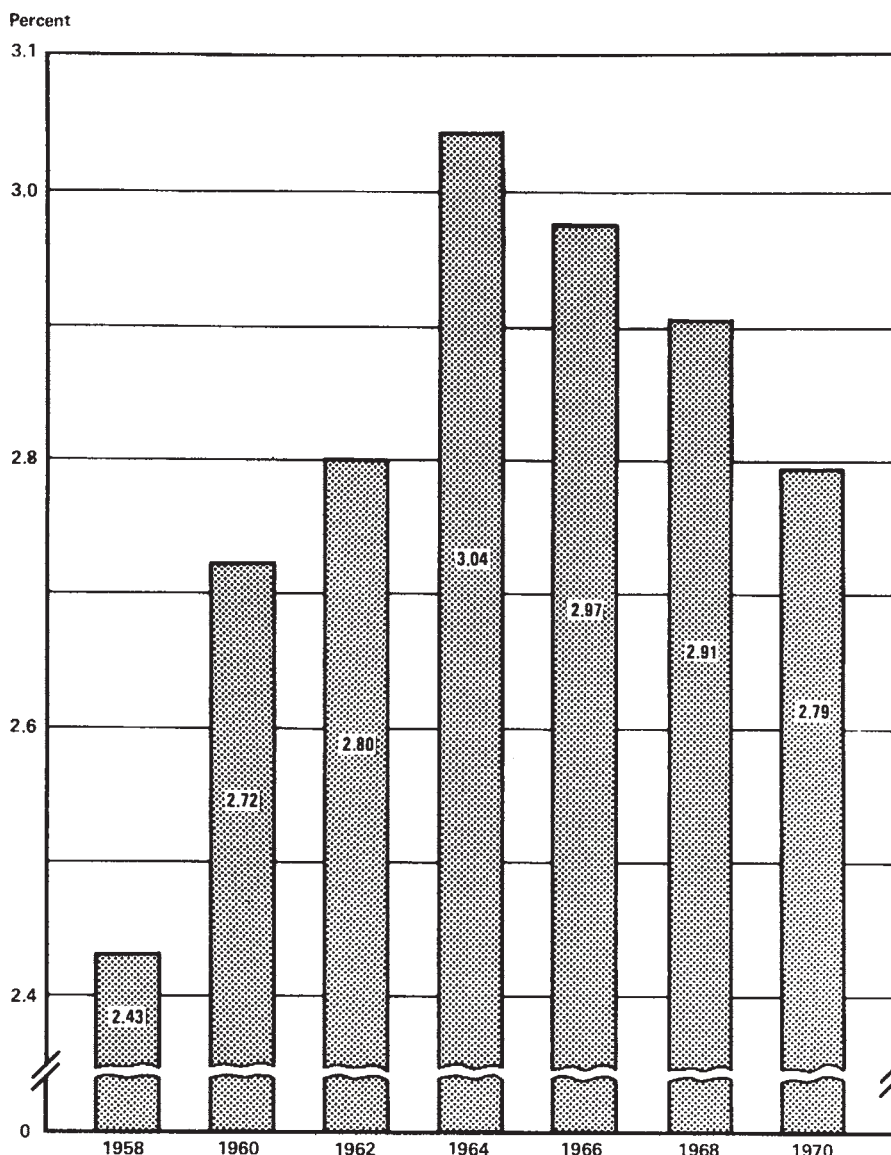
The theme of the AFL-CIO's argument, presented to the subcommittee by Mr Andrew J. Biemiller, a former congressman, is that uncontrolled foreign investment has enabled other nations to match the technology of the United States in some crucial areas. The upshot is that United States capital has stimulated other nations' economies and has provided job opportunities abroad, while unemployment in the United States has steadily been getting worse. In short, the AFL-CIO accused the United States

of exporting technology at the expense of home investment. Citing the textile industry as an example, Mr Biemiller pointed out that Asian textiles were no threat to the American market at one time because they could be relied on to shrink, but that situation was changed when the sanforization process was licensed outside America.

Economic isolationism is, however, unlikely to find many friends in Congress, and the AFL-CIO was given a fairly rough ride by the committee and by Murray L. Weidenbaum, assistant secretary to the Treasury for economic policy, at a later hearing. Referring to the ideas as "crude protectionism", Mr Weidenbaum said, "one

thing you don't do is to prevent the international movement of technology or inhibit licensing in that way". He pointed out in particular that the international flow of technology is a two-way process, and that the United States is also at the receiving end of some foreign technologies.

Mr Weidenbaum's own suggestion is that "what is needed is a relatively steady trend of funding for research—steady in 'real' terms to protect research budgets against the inroads of inflation". But, while it is relatively easy to plan the rate of funding for research and development in the public sector, the private sector is a much tougher nut to crack. And the impor-



Source: National Science Foundation

The ratio of expenditure on research and development to the gross national product, 1958-1970.

tance of providing sufficient incentives for research and development in the private sector is emphasized by the fact that about 85 per cent of the development part of R & D is performed by private industry, chiefly with financial support from the companies themselves.

Maurice H. Stans, Secretary of Commerce, left the subcommittee with a few suggestions to chew over, however. "We should examine," he said, "the feasibility of establishing a single federal focus for several activities directly related to enhancement, assessment, and forecasting of industrial technology." This suggestion is an echo of an old cause of the subcommittee's, which held a number of hearings last year under the former chairman, Emilio Q. Daddario, to explore the feasibility of setting up an Office of Technology Assessment, and which has recently been putting that into effect.

The second option suggested by Mr Stans is that the committee should carefully consider the feasibility of creating direct or indirect financial incentives to stimulate new technology. Federal assistance could be provided to private companies—for example by loan guarantees, cost sharing, grants or procurement incentives, and the risk of setting off to develop a new technology could also be offset to some extent by tampering with the tax structure, giving depreciation allowances, and a host of other indirect subsidies. And, taking a sideways glance at his own National Bureau of Standards, Mr Stans suggested that there could be considerable tightening up on the setting of industrial standards. "Potential manufacturers," he said, "hesitate to invest heavily in the introduction of innovative equipment when they are uncertain about the requirements or specifications which will define the market for such equipment, especially in export trade."

But voluntary standards made by private industry are likely to fall foul of the anti-trust laws. Although the overt reason for the anti-trust laws is to prevent the formation of cartels and similar price-fixing rings, they can also have the effect of slowing research and development, for with the exception of a few special cases it is illegal for companies to collaborate on research projects. Mr Stans suggested that "it may well be time to modernize the anti-trust laws which evolved to deal with the different problems of an earlier era in order to permit the pooling of funds and risks that must accompany major technological advances". He was also quick to point out when questioned by the committee that it is premature to draw the conclusion that changes in the laws are on the way. Nevertheless, it seems clear that in areas such as research and development on pollution control, some relaxing of the anti-trust

laws is being considered at least in the Department of Commerce.

Mr Stans told the subcommittee that in some areas American companies are being hamstrung by the anti-trust laws in such a way that they find it difficult to compete on equal terms with joint research projects conducted by their foreign competitors. But at home the anti-trust laws are increasingly becoming a source of concern for the smaller motor manufacturers who must meet stringent exhaust emission standards by 1975.

Mr Leonard Woodcock, president of the International Union, United Automobile, Aerospace and Agricultural Implement Workers of America (the union which represents most of the motor workers in the United States), wrote to Mr John N. Mitchell, the Attorney General, on May 24 suggesting that unless a crash programme combining the resources of all manufacturers in the automobile industry is conducted, the problem of exhaust pollution may not be solved before the 1975 deadline, and moreover, many of the smaller automobile companies are likely to go to the wall simply because they have insufficient funds to invest in pollution research. "This cooperative effort," he said, "can be maintained

within both the spirit and the letter of our anti-trust laws." But Mr Richard McLaren, Assistant Attorney General in the Anti-trust Division, did not agree, for in reply to Woodcock's letter he said "we cannot agree . . . with your statement that there should not be competition in such vital areas as human safety and pollution control. Competition has served us well as a spur to the enormous technological gains achieved in this and previous decades. It should not be abandoned as we strive to meet the critical challenges to the safety and health of American citizens".

Perhaps the best explanation of the policy of the Department of Justice towards collaboration on pollution research was given by Mr McLaren in a letter to Mr John A. Volpe at the Department of Transportation, when he said "the Department of Justice feels that government agencies which are charged with the responsibility of meeting specific public goals, such as promoting automobile safety, should proceed in a manner which promotes competition to a maximum extent consistent with the achievement of their specific statutory responsibilities". Obsolete or not, the anti-trust laws are plainly a fundamental part of the American industrial ethos.

Pesticides in the Open

A MUCH criticized obstacle to the free flow of scientific information about pesticides and herbicides was removed last week by Mr William D. Ruckelshaus, Administrator of the Environmental Protection Agency. The EPA has now decided to release scientific advisory reports on controversial pesticides as soon as it receives them. The reports, which often constitute an important part of the mechanism by which an allegedly dangerous agent is banned or allowed for use, have in the past been kept secret until a final decision is taken. This has made it impossible for the scientific information contained in the reports to be criticized or discussed by professional scientists until it is too late to affect the final decision.

The scientific advisory reports are filed under the provisions of the Federal Insecticide, Fungicide and Rodenticide Act, which allows a manufacturer of a product whose use has been cancelled by the EPA to request that the issue be referred to an advisory committee or to ask for a public hearing. This procedure can delay cancellation by six months or more, for the manufacturer has 30 days after the serving of a cancellation notice to request referral to the advisory committee and the committee, whose members are nominated by the National Academy of Sciences, has 60 days in which to make its report. Within 90 days, Mr Ruckelshaus must then decide either to confirm or to set aside his earlier notice of intention to cancel or suspend the product. During the whole of these proceedings, the manufacturer is allowed to market the product.

The issue of secrecy has been brought into sharp focus recently with the controversy surrounding a report on the herbicide 2,4,5-T, which was submitted to Ruckelshaus in May. A few copies of this have found their way into circulation, and it has come in for strong criticism from some sectors of the scientific community. One of the charges levelled at the report is that the scientific information which it contains would not be acceptable for publication in a scientific journal, because some of it is based on superficial experiments conducted without proper controls. That information will, however, now be open to criticism, for the 2,4,5-T report is available from the EPA upon request.

ATOMIC ENERGY

Seaborg to Leave AEC

by our Washington Correspondent

DR GLENN T. SEABORG, chairman of the Atomic Energy Commission for the past decade, will leave the AEC next year, probably in November, to return to the University of California at Berkeley. His resignation, which was announced recently, was obviously expected in the White House, for President Nixon wasted little time in making public his choice for a successor, and sent the name of James R. Schlesinger, an assistant director of the Office of Management and Budget and a lifelong Republican, to the Senate for approval. Seaborg pointed out in his letter of resignation that last year he expressed the desire to return to California to resume his research on transuranium elements—research for which he won the Nobel Prize in 1951.

Although Nixon accepted Seaborg's resignation "with regret", and was unstinting in his praise for Seaborg's record of achievements at the AEC, it has been suggested that he was looking for a change of leadership for the commission. During the past year, the AEC's nuclear energy programme has faced mounting opposition from environmentalists, and strong doubts have been cast on its nuclear safety programme. Nevertheless, Seaborg has skilfully ensured that the AEC's programme has gone forward largely unmodified, and there is little doubt that he has served the commission well during his ten years in office.

Seaborg is the president-elect of the American Association for the Advancement of Science, a position to which he was elected last December in the face of considerable opposition from some members of the association. The chief complaint raised against his candidacy was that as head of a much criticized government agency, he would find a conflict of interest in many of the issues with which the AAAS is involved—the issue of reactor safety which the AAAS was asked by Senator Edmund Muskie to investigate, for example. Few, however, opposed his election on personal grounds, and his resignation from the AEC may help to assuage those fears, although for the major part of his term of office at the AAAS, which starts on January 1, 1972, he will be wearing both hats.

Schlesinger, Seaborg's proposed successor, is widely regarded as a whiz kid in the Nixon Administration. A graduate in economics from Harvard, where he later obtained a PhD, he has been a member of the faculty of the University of Virginia, and immediately before joining the Nixon Administration in 1969 he was engaged

on a study of nuclear proliferation at the Rand Corporation. His first and only job in the Administration was in the old Bureau of the Budget and later in the Office of Management and Budget, where his chief area of concern has been defence spending, but he has also been involved with funding for environmental protection. He was also said to have been considered by Nixon for the post of Under Secretary for the Interior, but that suggestion was opposed by Republicans from the Western States, and his name was never put forward for nomination.

Environmentalists will be able to take some heart from the fact that his hobby is bird-watching. But as head of the AEC he will face a difficult task in resolving the conflict between environmentalists who oppose the nuclear power programme and the strong advocates of nuclear energy in the Congress and the Administration. Nixon will be looking to Schlesinger to put into effect the commitment to have a liquid metal fast breeder reactor in operation by 1980—an important part of the message to Congress in June in which Nixon requested \$3,000 million for a crash programme for developing clean energy. The decision to concentrate on nuclear power production at the expense of other possible fuels has met with considerable opposition from environmentalist groups, who are urging a closer scrutiny of the environmental and public health hazards from reactors. Schlesinger's job at the AEC will evidently be to make sure that the nuclear power programme is not seriously disturbed by such fears, although he must obviously satisfy his critics that he is not deaf to their warnings.



James R. Schlesinger, Nixon's nominee as AEC chairman.

Uranium Enrichment

A FUNDAMENTAL change of policy for the sharing of information on uranium enrichment was announced last week by the US Atomic Energy Commission. The AEC is prepared to enter into discussions with the governments of ten other nations to explore possibilities for cooperating in multinational uranium enrichment facilities. The AEC is quick to point out, however, that these talks "would not involve a commitment at this time on the part of the US to make such technology available for use abroad". The talks are therefore simply concerned with exploring the financial and security arrangements under which the United States may be prepared to grant licences for the operation of gaseous diffusion plants in foreign countries. The nations to be represented at the talks are Britain, France, West Germany, Holland, Belgium, Luxembourg, Italy, Australia, Canada and Japan.

The Joint Committee on Atomic Energy has long opposed any move towards the sharing of American gaseous diffusion technology with other nations, chiefly because it fears that the technological and economic lead that the United States now holds in this process may be lost, and some members clearly view the announcement with misgivings, for the committee has asked in no uncertain terms to be kept informed of developments. The commitment to enter exploratory talks is the fruit of a review of US policy on uranium enrichment conducted by the administration and announced by President Nixon in his foreign policy report to Congress on February 25.

The Atomic Energy Commission also points out that gas centrifuge technology will not form a part of the exploratory talks, so that the United States is not seeking to join Britain, West Germany and Holland in their multinational research effort on the gas centrifuge process (see page 360). An official at the AEC pointed out that the talks will be limited to gaseous diffusion because that process has already been proven, and it offers the best approach to meeting the demand for enriched uranium in the late 1970s.

This change in policy is bound to be welcomed by the nations involved, as it will expedite the use of uranium for peaceful purposes.

NEWS AND VIEWS

New Baskets for Old

UNICELLULAR organisms reflect the extremes to which cellular morphogenesis can be stretched, as any protozoologist will testify. However esoteric their appearance they also retain the ability for clonal growth—to generate repeatedly two “finished” cells from one. They, and indeed most cells, contain organelles made up of microtubules—arrays of globular protein subunits which form hollow tubes of diameters around 250 Å. Protozoa should therefore spell out the range of possible structures which can be formed from microtubules and yet be reduplicated in a spatially precise manner at each cell division. The control of such a system presents intriguing problems. On page 387 of this issue of *Nature* J. B. Tucker of the University of St Andrews, Scotland, raises questions about the spatial discrimination that must underlie the formation of microtubular components in the ciliated protozoan *Nassula*.

The largest organelle in *Nassula* is the feeding apparatus the pharyngeal basket), a palisade of rods made up from longitudinal microtubules and attached to the cell surface. At division the old basket detaches from the surface and two new ones appear. Each new rod begins its assembly close to a basal body, another and more ubiquitous microtubular structure. The rods first appear in short rows; they align and detach from the basal bodies and then roll up to constitute the circular palisade. The completed baskets make microtubular connexions to other surface basal bodies. The two new baskets do not always include all the new rods, and these “errant” rods, after moving away, break down as do the old rods, while the integrated new rods elongate by addition of microtubular protein to their tips. How can rods in one area of the cell add subunits while apparently identical rods elsewhere in the same cytoplasm are being dismantled?

Like flagella elongation in *Chlamydomonas* the synthesis and assembly of rod microtubules are separable events. Cycloheximide inhibits synthesis and colchicine blocks assembly. Errant rods do not move away from the new baskets in the presence of vinblastine, nor are they resorbed, although the old rods continue to break down. Tucker erects two alternative hypotheses to explain this effect. Further research relevant to this study will be the resolution of the number of different types of microtubule subunit involved, and whether the microtubular assemblies appearing at different times and in different places are composed of identical subunits, and if so whether these share a common subunit pool, and are recycled when the structures are broken down.

The questions that Tucker raises—how the subunits are localized at the points of assembly and whether random diffusion of subunits synthesized throughout the cell accounts sufficiently for the observations—are two among several problems. They include the nature of the information system specifying the location of “nucleation” centres for organelles, the number of such centres and the regulation of the dimensions of the realized structures, and the self-assembly properties of the subunits. Tucker has previously observed in living cells that rod length fluctuates with feeding and starvation and that when the

number of developing tubules is reduced they reach greater than normal length; both these facts are consistent with the available subunits determining the length. Dingle can upset the control of flagella number in *Naegleria* by heat shock at the moment of amoeboid-flagellate transformation (*J. Cell Sci.*, **7**, 463; 1970). The attraction of this system is that high developmental synchrony can be obtained in populations of these amoebae. Tilney (*Devel. Biol.*, **2** (Suppl.), 63; 1968) and Roth (*J. Ultrastr. Res.*, **30**, 7; 1970) have suggested that the pattern of microtubules in the axopod of the heliozoan *Echinospaerium* is a function of cross-linkages of fixed length and orientation between tubules rather than of an “orientation centre”. Heat-shock disruption of rod tubules in *Nassula* and the subsequent abnormal arrangements of tubules argue in favour of the initiating sites as the determinants of the final pattern.

The solution of these problems promises to be of interest to all cell biologists and it may in addition shed light on the phenomenon of “cortical inheritance” in ciliates—alternative patterns of the same microtubular structures existing stably over hundreds of cell divisions in the absence of gene differences. Finally, it would be a glaring omission not to point out the close affinity in interest and attack between this field and that of phage morphogenesis (Levine, *Ann. Rev. Gen.*, **3**, 323; 1969).

Filling the Dating Gap

THE dating of the earlier part of the Pleistocene period still presents considerable problems but further exploitation of the various “radioactive clocks” should eventually overcome these difficulties. It is particularly encouraging that thermoluminescence dating may soon be extended to date bones and teeth from archaeological deposits (Christodoulides and Fremlin, *Nature*, **232**, 257; 1971). The use of this method is well established for the dating of baked clay objects, and its potential for solving questions of authenticity has been illustrated in the past week by Martin Aitken and his colleagues at the University of Oxford who have demonstrated clearly that some “Etruscan” wall paintings on terracotta in European and American museums are at the most 12 years old (Aitken *et al.*, *Archaeometry*, **13**, 89; 1971; Fleming *et al.*, *ibid.*, 143).

The promise of the thermoluminescence dating method of Christodoulides and Fremlin is that it will span the gap which still separates the time range of radiocarbon dating and the clocks of longer half-life. At the early end of the human time scale, potassium-argon dating has been useful in establishing a chronology for artefacts or hominid remains. The youngest dates obtainable from the uranium-lead and rubidium-strontium methods are about 10 million years, so that these isotopes, which are useful for longer geological time spans are not helpful here. The half-life of ^{40}K is 1.03×10^9 yr, however and mass spectrometry allows the determination of one of its decay

products, the gas ^{40}Ar , in low concentrations. It is more difficult to date more recent ages than older ones because of the small quantities of argon involved, and the lower limit of the method is at present half a million years or a little less.

At the other end of the scale is radiocarbon dating. Radiocarbon dates now provide the essential basis for prehistoric chronology from Upper Palaeolithic times on and, until recently, radiocarbon seemed the most reliable of radioactive clocks. For a radioactivity-based age determination, it is usually necessary, of course, both to measure the quantity of the decay product present and the quantity left of the parent isotope. Radiocarbon dating was able to dispense with the former, because the original concentration of the parent isotope, ^{14}C , was assumed to be the same as the modern atmospheric concentration. The discovery that the atmospheric concentration of ^{14}C has fluctuated in recent millennia by up to 8 per cent of the present level has come therefore as something of a shock. The radiocarbon determination of dendrochronologically dated samples is now allowing the investigation of this effect back to 6000 BC, but its magnitude before this time remains uncertain.

The half-life of radiocarbon, approximately 5.7×10^3 yr, sets a more fundamental limitation on the age of samples which can be dated. The short half-life means that after a few tens of millennia there is very little radioactivity left in the specimen, and the counting of disintegrations in the sample is always complicated by a background activity caused by cosmic radiation which cannot be eliminated. Even the isotopic enrichment of gas samples only increases the effective time range of the method to a maximum of 70,000 yr.

Between the potassium-argon and radiocarbon dating methods lies a gap from 50,000 to 500,000 yr where other methods are required. Fission track dating is a possibility, especially when applied to volcanic glass. But like the potassium-argon method it gives the date of formation of the rocks under examination so that for more recent times, where the archaeological remains are not likely to be interstratified with eruptive deposits, this is a serious limitation. It is over this time range that thermoluminescence dating would be most useful.

Thermoluminescence dating depends on the principle that many minerals give off light when heated—the light emitted being proportional to the radiation dose experienced since the formation of the material. Archaeologically it has so far been principally applied to pottery and baked clay and the dating involves determining the radiogenic minerals in the clay as well as the thermolumin-

escence itself. The necessity of determining very small quantities of decay product (as in the potassium-argon method) or of the parent isotope (as in the radiocarbon method) is thus avoided. An early problem was how to eliminate light during the readout on heating, which derived from the energy used in pulverizing the sample. Fortunately, heating in an atmosphere of nitrogen considerably reduces this problem. Further improvement of this method came from the separation of different grain sizes in the pottery and an accuracy of less than 10 per cent is claimed for fine grain dating (Zimmerman, *Archaeometry*, **13**, 29; 1971).

Until recently the chief application of thermoluminescence dating has been in testing the authenticity of museum objects. The magnitude of the variations in atmospheric concentration of ^{14}C , suggested by tree-ring work, indicated a further useful line of approach, and the first TL results of Zimmerman and Huxtable on early neolithic pottery from the Balkans (*Antiquity*, **44**, 304; 1970) lend some support to the long chronology indicated by tree-ring work. Pottery was unfortunately not manufactured before about 7000 BC, but the

same authors have dated baked clay figurines from the Gravettian site of Dolni Vestonice to 33,000 BP (*Archaeometry*, **13**, 57; 1971). The thermoluminescence age is 15 per cent higher than the radiocarbon age, with a probable error of 10 per cent. The method thus offers a useful check on radiocarbon dates.

The materials most readily available from Palaeolithic deposits are flint and bone, and it is these which make the work reported by Christodoulides and Fremlin, and the work which is currently in progress on thermoluminescence dating of flint, so promising. Once again the chief problem is luminescence arising independently of the radiogenic thermoluminescence which is to be measured. Christodoulides and Fremlin have reduced this effect to the extent that useful measurements can now be made on samples older than 100,000 yr.

If further work succeeds in reducing this background thermoluminescence by another order of magnitude, the method may yet yield useful dates in, and beyond, the 8,000 to 50,000 yr range at present covered by radiocarbon dating, but not yet checked by dendrochronology.

Mechanism of Polarity in Dispute

THE mechanism of genetic polarity has of late become the centre of one of those controversies which occasionally enliven the literature and the coffee room. One camp holds that nonsense codons, by stopping the movement of ribosomes translating nascent messenger RNA molecules, prevent further transcription because transcription is coupled to translation. Members of the other camp argue, however, that nascent messenger RNA chains continue to be elongated after a nonsense codon at some early position has prevented ribosomes translating the messenger. They claim that because the newly made stretches of messenger are devoid of ribosomes they are rendered susceptible to attack by nucleases and are degraded.

In next Wednesday's *Nature New Biology* there are two articles which present conflicting data to succour members of both camps. Imamoto and Kano, who favour the first hypothesis, have studied the synthesis of *trp* operon mRNA in a strain of *Escherichia coli* with a temperature sensitive mutation in the structural gene for one of the 30S ribosome proteins, P10, which must be present for ribosomes to initiate translation of natural messengers. They present evidence which suggests that the overall rate of transcription of the *trp* operon in this strain parallels the rate of protein synthesis. At the nonpermissive temperature protein

synthesis is impaired and correlated with this synthesis of *trp* messenger RNA is arrested.

By contrast, a few weeks ago Morse and his colleagues reported in *Nature New Biology* (**231**, 214; 1971) experiments which suggest that messengers devoid of ribosomes are degraded by a previously undetected endonuclease. Morse and Guertin now report new experiments on the effect of starving *E. coli* of amino-acids on the polarity of polar nonsense mutations in the *trp* operon. Polarity is relieved when stringent cells carrying such mutations are starved; in other words, the *trp* mRNA distal to the polar nonsense mutation, which is rapidly degraded in the presence of an adequate supply of amino-acids is stabilized when amino-acids are in short supply. By contrast, when relaxed strains are similarly starved there is no relief of polarity; indeed polarity is enhanced.

Morse and Guertin suggest that because starvation of stringent cells results in the cessation of ribosomal RNA synthesis as well as protein synthesis nucleotides must accumulate, and this might well result, by some feedback control mechanism, in the inactivation of nucleases. Messengers although exposed might therefore survive. By contrast, when relaxed cells are starved ribosomal RNA synthesis continues even though protein synthesis is halted.

HISTORY OF BIOLOGY

A "Non-event"

from a Correspondent

It is a truth of history and an aspect of human behaviour that momentous occasions recalled in later life by men who took part often gain in grandeur and importance with the passing of time. A study of contemporary documents by J. W. T. Moody (*J. Soc. Bibliog. Nat. Hist.*, 5, 474; 1971) shows that the presentation of the Darwin-Wallace papers on natural selection to the scientific world on July 1, 1858, was no exception to this general rule. As Moody points out the occasion has been said to represent the beginning of a new era in scientific thinking—the beginning of modern biology or the Darwinian Revolution—but at the time of its presentation it was something of a non-event.

In the first place, the meeting at the Linnean Society at the critical day had been specially called by the president for the election of a new council member, but the opportunity was taken to deal with other business. A list of donations to the society's library and museum was read and there followed the election of the new councillor by ballot and a lengthy eulogy of the recently deceased vice-president, Robert Brown. Then the secretary read the text of the Darwin and Wallace papers on the laws which affect the production of varieties, races and species with an introductory letter from Sir Charles Lyell and Dr J. D. Hooker, and he followed by reading five other papers on miscellaneous and unrelated subjects.

According to the account of the event recollected by Hooker at the jubilee celebrations in 1908, only Darwin, Lyell, and Hooker himself, had any knowledge of the papers to be presented and Darwin for domestic reasons did not attend the meeting. Gage has noted (*A History of the Linnean Society of London*, 54; 1938) that at that date agenda were not sent to members, so the fewer than thirty members who attended the meeting can hardly have expected a momentous meeting. Hooker seems to have been the source of the impression that the audience was awed by the revelations read to them; in a letter thirty years after the event he wrote "the interest excited was intense . . . it was talked over after the meeting 'with bated breath'. Lyell's approval, and perhaps in a small way mine . . . rather overawed those Fellows who would otherwise have flown out against the doctrine . . .". Moody, however, suggests that the audience were not so much stunned by new ideas as they were overwhelmed by the sheer volume of information loaded upon them. No formal discussion took place at the meeting, the audience was

expected to switch its attention instantly from the Darwin-Wallace papers to "Notes on the organization of *Phoronis hippocrepis*", and it is suggested that boredom and bewilderment on a July afternoon, as much as Lyell and Hooker's advocacy, contributed to the overawed silence which greeted the unveiling of the concept of natural selection.

GALAXIES

Circular Polarization

from a Correspondent

DURING the past two years astronomers have discovered circular polarization in the radiation from a variety of objects. At Jodrell Bank, for example, Conway and Gilbert measured significant circular polarization at 49 cm wavelength from several compact sources (*Nature*, 227, 585; 1970), and a series of reports from Kemp and his colleagues has described the circular polarization in the light from white dwarf stars and planets (*Nature*, 232, 151; 1971). The range of possible observations is now expanded still further with a terse announcement in *IAU Circular 2343* that circular polarization has been successfully detected in the optical radiation from two extragalactic sources.

For many years observers have determined the magnetic fields in the Sun by measuring the circularly polarized components in spectral lines split by the Zeeman effect. At the Crimean Astrophysical Observatory, Severyn, Nikulin and Kuvshinov hooked up a modified solar magnetograph to their 100-inch reflector telescope, and monitored the light from the radio galaxy M87, quasar 3C 273 and a Seyfert galaxy NGC 4151. The condensed, superluminous nuclei in the last two objects

gave a positive result: the degrees of circular polarization are 1.2 ± 0.4 per cent for 3C 273 and 1.1 ± 0.3 per cent for NGC 4151. One X-ray source in the galaxy Sco X-1 was also investigated, but like M87 it gave a negative result.

There are several ways of obtaining circularly polarized radiation, but theorists will understandably want to see a more detailed report before any firm conclusions can be drawn from this new discovery. It is important in that it adds another method for investigating physical processes inside remote compact objects. It is already well established that the synchrotron mechanism may be responsible for the continuum radiation at optical wavelengths, and with certain geometries for the magnetic field a circular component is also introduced into the radiation. An encouraging step in this direction is given by the 49 cm results, where the synchrotron theory seems to satisfy the observations.

SEAFLOOR SPREADING

Chemical Rates?

from our Geomagnetism Correspondent

SEAFLOOR spreading rates vary from ridge to ridge at any given time and probably even vary with time for any given ridge. The first of these propositions is easy to prove because the patterns of magnetic anomalies close to oceanic ridges may be compared directly with the well-dated geomagnetic polarity-time scale derived from continental rocks of the past 4 to 5 million years. When this is done it clearly emerges that average spreading rates for the past few million years are different for different ridges; and thus it is safe to say that current spreading rates are also different. Direct evidence for the

Dybbuks and Tachyons

A FEW years ago a suggestion was made that there might exist particles that travelled with a velocity greater than light. These particles, named tachyons, satisfy the fundamental equation of special relativity:

$$E^2 - P^2 = M^2$$

where E , P and M are the energy, momentum and mass of the particle. They differ, however, from ordinary particles in that their mass is imaginary but they have a real energy and momentum. In next Monday's *Nature Physical Science*, Raymond Fox of Haifa, Israel, points out that particles with imaginary mass, imaginary momentum and imaginary energy are also solutions of the fundamental

equation, and Fox names such particles "dybbuks". The one important difference between tachyons and dybbuks is that whereas it has been argued that the concept of tachyons violates causality there is no likelihood of such a problem with dybbuks.

Fox gives a description of the possible interactions of these particles and applies the results to an evaluation of the gravitational interaction of a very dense star. An interesting prediction is that the gravitational radiation from a pulsar is very much less than presently estimated. Such a prediction is bound to arouse interest in astronomy circles and the basis of Fox's theory will no doubt be subject to intensive study.

second proposition is more tenuous, however, because it is difficult to assign ages beyond about 5 million years to either the continental reversal pattern or the series of oceanic magnetic anomalies. Nevertheless, although the uniform spreading rate is sometimes used as a working hypothesis in geophysics, there is now quite convincing evidence that spreading rates do vary with time.

The need to determine spreading rates as a function of time has led Bass (*Earth Planet. Sci. Lett.*, **11**, 18; 1971) to take the first steps in a novel approach to the problem. The point of his argument is that if it can be shown that the chemical composition of the basalt extruded at ridge crests varies systematically with spreading rate at the present time, then it might be possible to determine the relative spreading rates for older oceanic crust by chemical analysis. He has thus tried to demonstrate that such variations exist.

The first thing to be said about this approach is that there are known to be practical difficulties both in demonstrating composition-spreading rate correlations and, supposing such correlations exist, in extrapolating them to older rocks. It is an experimental fact, for example, that any dredge haul of basalt from the ocean floor is likely to contain more than one type of basalt. It thus becomes difficult to assign a particular chemical characteristic to any area, or even site, of the ocean floor. But even if this problem can be overcome by the selection and use of suitable criteria, the application of those criteria to older crustal basalts is likely to be invalidated by the possibility of secondary alteration. It is too soon to say whether or not alteration will ultimately prove to be an insurmountable objection to Bass's method; but Bass has, at least, been able to show that there are systematic relations between chemical composition and spreading rate although he admits that the data are "too sparse to establish a statistically compelling argument" for strong correlations.

The ridges Bass has chosen to examine are the rapidly spreading East Pacific Rise and Juan de Fuca Ridge, the moderately slowly spreading Gorda Ridge and the slowly spreading Mid-Atlantic Ridge. Not all samples from these ridges were accepted in defining the chemical characteristic for each ridge—several classes of rock which would have led to ambiguities in interpretation were excluded. But when the compositions of the rocks selected by Bass are plotted on the normative AN-OL-HY ternary diagram, systematic variations in the positions of the fields for the various ridges became apparent. Thus the fields for the ridges of lower spreading rate move progres-

sively towards higher AN and OL values and the ends of the fields poorer in HY move progressively towards the AN corner. In short, the lower the spreading rate the richer in Al_2O_3 and the more undersaturated are the basalts.

According to Bass, the important conclusion to be drawn from these properties is that the lower the spreading rate for a ridge the greater is the depth from which magma can be derived. Thus if the maximum depth from which magma may be derived is, in effect, the maximum depth at which brittle fracture may occur, slowly spreading ridges must be underlain by thicker lithosphere. In other words, magma type or the chemical characteristics of the basalts may in principle be used as an alternative to seismic methods to determine the relative lithospheric thickness.

The correlation of lithospheric thickness with spreading rate then leads to conclusions about the processes which determine the maximum depth of brittle fracture. Whether the ridge is produced by stresses involved in the upwelling mantle material or by stresses imposed by the lithosphere sinking into trenches, the depth of brittle fracture (which determines the apparent thickness of the lithosphere) will increase with an increase in the rate of application of stress and thus with an increase in spreading rate. But working in the opposite sense is the effect of the geothermal gradient. The greater the spreading rate the greater will be the quantity of mantle material

entering the ridge region from below and so the greater will be the heat flow. The higher geothermal gradient will effectively reduce the depth of brittle fracture. Although it is not possible to predict which of these processes will take precedence, Bass's correlation of the thickness-spreading rate in the lithosphere enables the relative effects of the two processes to be determined. Thus because increased spreading rates lead to thinner lithosphere it means that the geothermal gradient effect dominates.

HAEMOGLOBIN

Structural Variants

from our Molecular Biology Correspondent

SINCE Pauling's discovery rather more than twenty years ago of sickle-cell haemoglobin—the manifestation of what with unerring flair he dubbed a molecular disease—well over a hundred human haemoglobin variants have been documented. Some, but by no means all of these, are associated with pathological conditions, and a comparison of the stereochemical features of such species in the crystal with those of the normal protein should, one might hope, lead to a precise explanation of how a single-base mutation can encompass such dire physiological consequences. With the biochemical world still digesting the implications of his results on the relation between the structures of oxy- and deoxyhaemoglobin, Perutz, together with Greer, has recently embarked on

Uniaxially Reinforced Nylon Composites

IMPROVING the mechanical properties of polymers by inclusion of comparatively high strength and modulus fibres, such as glass or carbon, is well known. Unfortunately not all polymers are amenable to this method of reinforcement for, to utilize to the maximum the good mechanical properties of the fibres, the composite needs to contain long lengths of fibre. Any method of moulding such as by injection or extrusion, where there is drastic deformation and movement, will thus cause damage to induced fibres and so reduce their reinforcing effect.

The reinforced polymers which have had the greatest impact in engineering have therefore been constructed with thermosetting materials, such as epoxy and polyester resins, which require only simple "static" moulding conditions. The reinforcing fibres are placed in the mould with the desired orientation. Liquid resin is then added in the form of monomer or oligomer containing catalyst and the mould is heated. Polymerization then occurs and a solid

moulding is formed. It is essential that no gaseous byproducts are produced during polymerization, for this causes disruption of the composite. Nylon is a well established engineering material which would benefit from fibre reinforcement. Some success has already been achieved by the incorporation of fibres before injection moulding, but fibre lengths in the composite are usually less than 1 mm and are almost randomly oriented.

Attempts to produce composites by this method of reinforcement fail because charging the mould with molten polymer is impracticable, and if normal monomers are used, water is evolved as steam during polymerization. But T. Bessell, D. Hull and J. B. Shortall report in next Monday's *Nature Physical Science* that this problem has been overcome by using caprolactam as the monomer and by inducing the ring opening type polymerization with anionic catalysts, so that the problem of gaseous byproducts is almost eliminated.

such studies of pathological variants (*Nature New Biology*, **230**, 261; 1971), and now Greer has contributed two new investigations of different types of structural aberration. To anybody except the young, the excessively blasé and the punch-drunk, they compel awe and fascination.

In the first article (*J. Mol. Biol.*, **59**, 99; 1971), Greer uses the difference Fourier method to study the structural effects of two different substitutions at a single position in the β -chain. Asn-102 is conserved in all known animal β -chain sequences, and may therefore be supposed to admit of little genetic tinkering. In haemoglobin Kansas, however, it is replaced by threonine, which causes the loss of cooperative function, and a decrease in oxygen affinity at physiological pH; in haemoglobin Richmond it is replaced by lysine, without any clinical penalty.

The difference electron density map of deoxygenated Kansas shows a disturbance near the β -haem group, for the threonine causes crowding at a vinyl and methyl side chain. The haem is displaced, and with it the helix to which it is linked by way of the histidine iron ligand. This has other consequences, including a distortion at the interface of the α_1 and β_1 chains which affects even the α -chain structure at various points, including the haem surrounds. The threonine cannot fulfil one of the functions of the asparagine, of hydrogen bonding to an α -chain aspartate, and appears instead to form an intra- β -chain bond. In haemoglobin Richmond, the distortion of the structure under the influence of the substitution is much less, and the lysine is even able to bond to the α -chain aspartate. A consequence of one of the new contacts is to displace another arginine, which normally shows a prominent interaction with an α -chain tyrosine. Possibly for this reason the Richmond molecule dissociates much more readily than normal haemoglobin into dimers. In haemoglobin Kansas, in which an important saltbridge is absent, and the structure is generally distorted, this effect is still more pronounced.

Greer's second article (*ibid.*, 107) concerns itself with two haemoglobin M forms, Hyde Park and Iwate. The M variants are characterized by substitutions for haem-linked histidines, the corresponding haem groups being then inert with respect to oxygen, and normally in the ferric form. Haemoglobin Iwate has an α -chain substitution, and Hyde Park a β -chain, histidine being in both cases replaced by tyrosine. The chemistry of these forms shows many peculiarities—in one of them, for example, the isomorphous replacement by a mercurial occurs at the wrong thiol. The Hyde Park variant moreover has a tendency to shed its α -haem groups and in a proportion of the molecules in

the crystal of the fully reduced pigment (and no doubt in solution) the haem is missing and its cavity is collapsed. The disturbance is localized, however, and is not transmitted to the rest of the molecule. Neither the aberrant tyrosine nor the distal histidine in this molecule approaches the haem.

In the α -chain Iwate variant the α -haem iron is evidently linked to the tyrosine and the normal distal histidine. The most striking feature of the structure in both the fully ferric and the β -deoxy-forms is that it is fixed in the deoxy-configuration, in spite of well-defined changes in the β -chain when its haem is liganded. This rationalizes the striking difference between the two M variants, Hyde Park having both normal oxygen affinity in its functional haems and a Bohr effect, and Iwate a low oxygen affinity and no Bohr effect. Evidently the tyrosine-iron bond prevents the normal steric transition to a state favouring the transition to the high-affinity quaternary structure, which, one may infer, originates in the α -chains. Molecular pathology aside, the particular value of these studies, especially when details can be seen at higher resolution, will be to reveal the nature of the intermediate states between the fully reduced and fully oxygenated forms, which could not otherwise be observed by crystallography.

STRATIGRAPHY

Fixing a Boundary

from a Correspondent

It cannot be often that the Red Army is responsible for a geological article. In August 1968 the International Commission on Stratigraphy met in Prague and was about to consider a proposal that the boundary between the Silurian and the Devonian should be fixed at the base of the *Monograptus uniformis* Zone, which is appreciably below the traditional base of the Devonian in Russia and Czechoslovakia, but unfortunately well above its base in Britain. The practical consequence of this in the classic area of the Welsh Borderland would be to transfer the lowest Devonian strata as originally defined by Murchison to the Silurian system. The support for the proposal suggests that it would have been accepted had the work of the commission not been interrupted. Because of the invasion, however, the matter is still open to debate. Westoll, Shirley, Dinley and Ball have recently taken advantage of this respite to argue (*J. Geol. Soc.*, **127**, 286; 1971) that the traditional position of the boundary between the two systems should be retained.

This may seem a rather arid discussion of interest solely to specialists. In

Marine Bands and Tonsteins revealed in Derbyshire

THE Westphalian Coal Measures are remarkable for the continuity and persistence of certain rock types, especially the marine bands which have characteristic fossil fauna resulting from relatively short lived but widespread marine invasions of the coal delta. These bands have long been accepted as reliable stratigraphic markers on which to subdivide and to correlate the coal measures of the British Isles and Europe. The thin, curious, kaolinitic bands called tonsteins discovered more recently in the coalfields of Western Europe have provided welcome additional markers for correlation purposes.

Tonsteins were first found in North Staffordshire in 1961 and discoveries in other British coalfields have followed, particularly at one horizon below the equivalent of the *Edmondia* Marine Band. They are usually only a few centimetres thick, yet some of them are traceable over hundreds of square miles and, as in the case of some marine bands, a few can be traced throughout the coalfields of Western Europe. Their origin is problematical and probably varied; the volcanic ash idea is attractive in terms of widespread persistence but it is also

held that they are the result of special soil forming processes.

In the forthcoming issue of *Nature Physical Science*, M. A. Calver, who has been associated with many discoveries of new marine bands in British coalfields, is joined by B. C. Worssam and G. Jago to demonstrate again that continuous core drilling coupled with examination can still reveal hitherto unproved marine bands and tonsteins. A series of boreholes drilled in the Pottery Clays of the South Derbyshire Coalfield during 1970 on behalf of the Institute of Geological Sciences and the National Coal Board have added considerably to the knowledge of the stratigraphy of these coal measures. Above the Overseal Marine Band Calver *et al.* have recorded the presence of the marine bands equivalent to the Top, Shafton and *Edmondia* Bands of the East Pennine Coalfields and they have also recorded a tonstein which occurs a little below the last of these bands at about the position of the Sub-High Main tonstein; another new tonstein is located between the Top and Shafton marine horizons. The elusive marine bands between the Overseal and underlying Two Foot have also been found and correlated.

fact, it arises from a more important philosophical question—how geological time should be measured. When stratigraphy was in its infancy, it was natural to fix on spectacular events the effects of which were readily apparent and to use these for dividing the geological record.

More recent ideas on the philosophy of stratigraphy, however, suggest that time is a continuum, and that stratigraphic boundaries are merely arbitrary divisions, much as the hours of the day are arbitrary. Once a boundary is agreed, and defined by a type section, stratigraphers can get on with their real business—correlation. From this it follows that type sections should be chosen in areas where the rocks have all the features useful in correlation—good varied faunas (preferably marine) and as few obvious breaks as possible. This means that the traditional type sections of the Silurian/Devonian boundary in the Welsh Borderland just will not do—not only are half the rocks continental, but the famous Ludlow Bone Bed represents a marked time break. A very suitable type area seems to be the Barrandium Syncline near Prague, which was protected from the major movements of the Earth which disturbed north-west Europe in early Devonian times and where the graptolites, all-important in correlation, were not forced to extinction.

Geologists are agreed that the new proposal presents British stratigraphers with some difficulties, as Westoll and his colleagues point out. They suggest that the boundary should be fixed at another graptolite zone rather lower in the succession, marked by *Monograptus ultimus*, which would give a boundary very close to the position of the Ludlow Bone Bed.

Not all their British colleagues take this view; there is considerable British support for the new proposal. It will be interesting to see whether Westoll, Shirley, Dinley and Ball are fighting a rearguard action or starting a successful counter attack.

OLFACTION

Smells Left and Right

from our Membrane Correspondent

IT has been reported that compounds, which differ only in their stereochemical configuration about one carbon atom, have distinguishably different odours. It is possible, however, that the difference in smell between these enantiomers can be attributed to that bugbear of olfactory research, the presence of unidentified impurities.

Earlier this year Leitereg *et al.* (*Nature*, **230**, 455; 1971) presented good evidence that the optical isomers (+)- and (–)-carvones, prepared

from both natural and synthetic sources, have different odours—caraway and spearmint respectively—but these authors still paid lip service to the possibility that the odour difference was caused by impurities. This possibility has now been convincingly eliminated in some recent work reported by Russell and Hills (*Science*, **172**, 1043; 1971) and by Friedman and Miller (*ibid.*, 1044).

Russell and Hills investigated five different enantiomeric pairs of compounds—(+)- and (–)-carvones and four derivatives of each of these. The actual samples used for odour evaluation were purified fractions which were collected after successive passages through two different gas-liquid chromatography (GLC) columns. In each case there was a highly significant difference in odour quality. Using GLC and a variety of synthetic pathways, Friedman and Miller investigated eight different enantiomeric pairs which had distinct odour differences. All but one (amphetamine) of the pairs were terpenoid compounds and these included the carvones and also (+)- and (–)-limonenes; the last two had the odour of oranges and lemons respectively—as in the case of the carvones this is a far from subtle difference in odour. Friedman and Miller paid particular attention to the carvones; they resolved

a racemic mixture, synthesized them by two different routes and also subjected them to a cycle of reactions which interconverted the + form to the – form and back again. The final products of all these manipulations were subjected to odour evaluation. The odours of the + forms were indistinguishable from each other as were the odours of the – forms, but the + and – pairs always had a significant difference in odour.

The postulated impurities now come to have unbelievable properties. There would have to be a different pair of impurities for many of the enantiomeric pairs studied, and in each case these impurities must survive both the GLC purification and the wide variety of chemical manipulations. Furthermore, just the same impurities would have to be present in both natural and synthetic compounds.

The vibrational and rotational modes of enantiomers are identical so that the now clearly established fact that enantiomers can have different odours spells death to any theory of olfaction which looks for correlations between odour quality and infrared spectra. Furthermore, other theories are now faced with the task of explaining why some enantiomeric pairs have different odours and other pairs have identical odours.

Some Pulsars May Emit Thermal X-rays

THE view that pulsars may consist of a superfluid core of neutrons surrounded by a rigid crust, as suggested by Baym, Pethick, Pines and Ruderman, is examined by George Greenstein of Princeton University Observatory in next Monday's *Nature Physical Science*. So far the attraction of the model of Baym and his colleagues has been that it accounts in a neat way for some of the irregularities in the behaviour of pulsars, interpreted in terms of starquakes occurring in the rigid crust. In this model the slowdown of the spin of the pulsar is accompanied by frictional heat as a result of slippage between the crust and the core.

Greenstein has evaluated the magnitude of this heating, which is on top of the temperature expected for pulsars on the basis of cooling theory, so that the temperatures which he obtains from an examination of the slowdown of pulsars can be considered as lower limits to pulsar temperatures.

It will not come as a surprise that the two pulsars for which the frictional heating process seems significant are the two fast pulsars, in the Crab Nebula and in Vela. For both these objects Greenstein finds temperatures caused by frictional heating arising between the rigid crust and neutron superfluid of 10^6 K. He suggests therefore that

thermal X-ray emission ought to be detectable from these two objects—he expects them both to have X-ray fluxes of the order of 3×10^{-27} erg cm $^{-2}$ s $^{-1}$ Hz $^{-1}$.

It may also be possible to detect the thermal X-ray flux of 1×10^{-28} erg cm $^{-2}$ s $^{-1}$ Hz $^{-1}$ that is expected from what is thought to be the closest pulsar, CP 0950. Another possibility is that pulsars the orientation of which is such that their pulsations are not detectable at the Earth may be discovered by their thermal X-radiation.

But for other pulsars the expected thermal X-ray emission is appreciably weaker— 1×10^{-30} erg cm $^{-2}$ s $^{-1}$ Hz $^{-1}$ for HP 1508 and 3×10^{-29} erg cm $^{-2}$ s $^{-1}$ Hz $^{-1}$ for CP 1133. For these two objects the expected associated visual magnitudes are 32 and 27 respectively, far beyond the capabilities of the best optical telescopes.

Greenstein also reports that the heating at the inner boundary of the core takes place in a thin shell that can be a kilometre or so, or less, in thickness. He also points out that his equations indicate that fluctuations in the temperatures of pulsars are mirrored by corresponding fluctuations in the periodicity of the pulses, so that the regularity of pulsars implies that their temperatures are also kept amazingly constant.

NUTRITION

New Protein Foods

from a Correspondent

THE conference at the University of Reading, from July 13 to 15, on the topic of new protein foods differed from many others on the same subject in that it was confined to agricultural conditions in the United Kingdom. In his introduction, Professor F. Aylward (University of Reading) classified the different kinds of new protein foods and stated that a crop for the production of protein concentrates depends in practice on a combination of factors including (1) yield of protein, (2) technical problems of harvesting, extraction and processing, (3) nutritional value of protein and freedom from anti-nutrient or toxicological factors, (4) acceptability of product for direct use as a food or as a food component, and (5) economic and commercial considerations. The yield of protein depends on the percentage of protein in the crop, the total yield of crop, the actual yield of protein after harvesting, and the yield after processing.

Dr R. R. Robinson (University of Reading) described the use of bacteria, yeasts, fungi and chlorophyll-containing plants such as unicellular algae. There are many difficulties to be overcome regarding the extraction of protein from these organisms and oilseeds, legumes and cereals are likely to be the chief source of protein during the next two or three decades. Dr B. J. F. Hudson (University of Reading) ventured to predict the possible increase in consumption of these foods in the United Kingdom up to AD 2000. On the basis of careful calculations by forty different experts it seems that textured proteins and similar plant protein concentrates might replace as much as a quarter of the meat by AD 2000, or even earlier. Professor H. M. Sinclair (University of Oxford) dealt with the nutritional potential of these new protein foods. He emphasized the importance of ensuring a sufficient content of vitamin B₁₂, with fortification if necessary, and pointed out the valuable clinical work which is being carried out on vegans living only on plant foods.

Dr M. A. Crawford (Nuffield Institute of Comparative Medicine, London) emphasized the importance of other factors besides protein in the new foods and drew attention to the role of structural phospholipids in the brain and other parts of the central nervous system. Both Professor Sinclair and Dr Crawford said that the correlation between too high a level of total phospholipids and nervous diseases seems to be connected with the phospholipids breaking down, but they did not state the cause.

Meat production and demands in the

United Kingdom were described by Mr H. F. Marks (Meat and Livestock Commission) and Dr A. M. Ashby (Unilever Ltd). Although Britain's entry into the Common Market would be expected to cause rises in meat prices probably greater than the corresponding income rises, they thought that the total consumption of meat would not fall much, although they agreed that much more consumption of these new protein foods will gradually develop. Dr W. F. Raymond (Grassland Research Institute, Hurley) suggested that the high cost of meat production might be curbed to some extent by using alternative feeding stuffs including perhaps those made from microorganisms.

Dr M. A. B. Boddington (Wye College, London) applied land use projections for the next 30 years to forecast possible developments in yields from land which might improve the present low conversion efficiency of only 6 per cent for beef and 12 per cent for pigs.

REVERSE TRANSCRIPTASE

Templates for Caution

from our Cell Biology Correspondent

As Spiegelman in particular has of late taken great pains to emphasize, enzymatic activities detected by their ability to use synthetic RNAs and RNA/DNA hybrids as templates for the synthesis of DNA cannot be immediately equated with the reverse

transcriptases found in animal tumour viruses. The enzyme or enzymes in such viruses—and there is still some dispute as to whether or not a single enzyme molecule can complete the synthesis of a double stranded DNA from the single stranded RNA viral genome (Robinson and Robinson, *Virology*, **44**, 457; 1971)—use endogenous viral RNAs, synthetic RNAs and hybrids as templates for the synthesis of DNA. But it does not inevitably follow that all enzymes which *in vitro* can be programmed by synthetic RNAs or hybrids to polymerize deoxynucleoside triphosphates function *in vivo* as authentic reverse transcriptases and have an endogenous and natural single stranded RNA template. Synthetic nucleic acids are useful templates for the detailed investigation of reverse transcriptases once the enzymes and their natural templates have been identified, but the identification of a reverse transcriptase in a new situation depends on the identification of its natural template.

Indeed if the ability of an enzyme to use synthetic RNA as a template for DNA synthesis *in vitro* is taken to be diagnostic of its function *in vivo* as a reverse transcriptase, the Kornberg DNA polymerase I of *Escherichia coli* must be classified as a reverse transcriptase. For as long ago as 1963–4 Cavalieri and his colleagues proved that DNA polymerase I can utilize double stranded synthetic RNAs as

Oncogenicity of Cleaved Adenovirus DNA

ALTHOUGH the adenoviruses apparently cause nothing more devastating than respiratory infections in their natural hosts, at least some of them induce tumours when they are injected into newborn rodents and will transform some of the cells which they infect *in vitro*. Attempts to analyse genetically the oncogenes in adenovirus genomes, by the isolation of temperature sensitive mutants, seem most promising, but meanwhile Mayne, Burnett and Butler have set about the physical isolation of fragments of the simian adenovirus 7 (SA7) genome which contain these genes. Next Wednesday's *Nature New Biology* contains their progress report.

Having first shown that intact DNA isolated from SA7 is not only infectious but capable of inducing tumours when injected into newborn hamsters, they have now fragmented this DNA, either by sonication or by shearing it through a syringe, fractionated the fragments and tested their oncogenic potential. Molecules roughly half the size of the complete genome, which can be separated by virtue of their density into heavy

and light halves, induce tumours like intact molecules. By contrast smaller fragments obtained by sonication are not oncogenic.

The induction of tumours by both heavy and light "half" molecules, but not by smaller pieces, is of course disappointing to anybody bent on physically isolating the SA7 oncogenes free of any other genetic material. For although these experiments prove that the whole genome is not essential for oncogenicity the fact that both halves of the genome have oncogenic potential may well mean that several regions of the genetic material, rather than a unique segment, contain oncogenes. Alternatively and more optimistically, it might be argued that the oncogenes are centrally located in a small segment of the genome, which, depending on the precise point of cleavage, might be included in either the heavy or the light "halves". The hybridization studies between "half" molecules and DNA extracted from the cells of tumours induced by heavy and light "halves" that Mayne *et al.* promise may perhaps resolve this issue.

well as single stranded natural RNAs as templates for DNA synthesis. And, rubbing home the message, Cavalieri and Carroll reported two weeks ago in *Nature* (232, 254; 1971) that the addition of traces of calf thymus DNA to *E. coli* ribosomal RNA resulted in a three to ten-fold increase in the incorporation of the four deoxynucleoside triphosphates catalysed by *E. coli* DNA polymerase. This result is, of course, entirely reminiscent of the stimulatory effect of Goulian pieces on DNA synthesis catalysed by DNA polymerase I with natural DNA templates.

Mindful of these findings, it is perhaps rash of Werner *et al.* (*Biochem. Biophys. Res. Comm.*, 44, 433; 1971), who have found that skin cells from people with xeroderma pigmentosum contain an enzymatic activity, which uses poly rG.dC as a template for DNA synthesis, that is absent from normal human skin cells, to conclude that xeroderma pigmentosum skin cells are infected with a tumour virus and contain a reverse transcriptase. In the light of Cavalieri's experiments and Spiegelman's cautionings one can offer an equally plausible alternative explanation of the data Werner *et al.* present.

There can be no questioning the fact that xeroderma pigmentosum cells lack some if not all DNA repair mechanisms and fail to excise pyrimidine dimers. Moreover this defect may well be responsible for the greatly enhanced incidence of skin carcinomas among people with xeroderma pigmentosum. Perhaps the different responses to poly rG.dC and native DNA of extracts of normal and xeroderma pigmentosum cells, which Werner *et al.* have detected, are the result of a mutation which has changed the template specificity of the cell's DNA repair enzyme(s). If human DNA repair enzymes resemble *E. coli* DNA polymerase I they will no doubt be induced to use, in the highly artificial environments set up by biochemists, synthetic RNAs and DNA/RNA hybrids as template. It does not take much stretching of the imagination to picture a mutation which would cause such an enzyme to use RNAs and hybrids in such experimental conditions in preference to native DNA, and at the same time impair DNA repair *in vivo*.

CONSERVATION

Rhinos Survive

from a South African Correspondent

DURING the early history of South Africa at least two big game species, the true quagga, *Equus quagga*, and the bluebuck, *Hippotragus leucoph-*

aeus, were exterminated and many other species were severely curtailed in numbers and distribution. The approach to these matters has now improved considerably, however, as is shown by two recent reports.

One report by Dr U. de V. Pienaar, Nature Conservator of the Kruger National Park, points out (*Koedoe*, 13, 157; 1970) that the southern white (or squarelipped) rhinoceros, *Ceratotherium simum*, is now safely re-established in the park after having been extinct in the eastern Transvaal for 65 years. The last white rhino in this area was apparently shot around 1896, when it seemed to be heading for extinction throughout its range. But it survived in the Umfolozi-Hluhluwe corridor complex in Zululand and gradually recovered so well that a danger arose of over-utilization and destruction of the available habitat. As long ago as 1928 the possibility of translocating rhino from Zululand to other parts of their former range was suggested by the naturalist Herbert Lang, but it was not until about 1960 that it became feasible for the Natal Parks Board to undertake large scale translocation. Even so, more than 1,200 animals remain in the Umfolozi-Hluhluwe corridor complex, so that the threat of over-utilization of the habitat has not been averted.

The second report, by Dr W. von

Richter of the Mammal Research Unit, University of Pretoria (*Ann. Transv. Mus.*, 27, 35; 1971), discusses the present status of the black wildebeest, *Connochaetes gnou*. This animal originally occurred extensively in the central open plains of South Africa, particularly the highveld grasslands of the southern Transvaal, Orange Free State and Karoo and the central and southern Cape grassveld. In addition it was probably a seasonal migrant into Natal. Within its range it was initially extremely abundant, but indiscriminate hunting, together with periodic disease outbreaks and gradual curtailment of the habitat to make way for human settlement, caused it to dwindle to about 600 animals, chiefly in the Orange Free State and southern Transvaal, by the turn of the century. Since then, however, numbers have increased steadily to more than 1,000 in 1945, about 1,800 in 1965 and 3,100 in 1970, as well as more than 155 animals living in zoological gardens in various parts of the world. The most marked increase has been in the Transvaal.

Von Richter concludes that, whereas it was thanks to the initiative of a few farmers that the black wildebeest was saved from extinction, an important factor in its survival has been the establishment of breeding herds in the national parks and provincial reserves.

Structure and Base Composition in DNA

IN the next issue of *Nature New Biology*, Bram contradicts the crystallographic dictum that DNA conformation is essentially independent of base composition. From X-ray scattering envelopes on gels or concentrated solutions, Bram previously found that the conformation of a DNA of typical base composition was little different from the B-structure found in fibres at high humidity. The same was true for DNA within calf thymus nucleohistone. A comparison of observed with calculated scattering curves indicated a small difference in the helix twist from that of B-DNA. Bram has now examined two bacterial DNA species containing 67 and 69 per cent of (A+T), as well as the alternating polymer, poly d(AT), and he reports that these do not fit the same model. The axial radius of gyration is similar, but the cross-section of the AT-rich species has much greater anisotropy. The curves fit neither a B nor an A nor a C-type of model, but all that can be said about the geometry of the new structure at the present stage is that the helix pitch is some 10 per cent larger than that of DNA of lower AT content. Bram suggests that the difference may be in the pucker of the sugar ring.

Bram notes that the transition of the DNA structure between the two forms is highly cooperative, in the sense that a large structural difference is observed between molecules containing 56 per cent and 67 per cent (A+T), but as between 56 per cent and 28 per cent (A+T) there is no further detectable change. Whether this apparent disagreement with earlier X-ray diffraction studies on fibres is a result of inadequate diffraction data on high-AT species, or on differences between the fibre and solution states, remains to be established.

The biological implications of the findings that Bram reports may well be profound. If, as he suggests, AT-rich regions in a single chain cause alternation between the two types of structure, this offers a basis for a whole series of protein recognition processes. Some enzymes, repressors, and such molecules as polylysine, all show a strong binding preference for DNA species rich in (A+T). In bacterial DNAs tracts extremely rich in (A+T) have in fact been found. The observations would also make necessary a re-examination of the dependence of spectroscopic and other properties of DNA on the base-composition. The possibility exists that a similar effect may occur in RNA.

Value of Historical Records of Earthquakes

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Modern earthquake catalogues have been found unreliable in reporting earthquakes which occurred before 1900, because of a series of errors perpetuated at second and third hand. A new study of the original records provides significant data relating earthquake activity in the Eastern Mediterranean basin with plate tectonic activity over the past 2,000 years.

It is now recognized that any hope for earthquake prediction rests on increasing knowledge of earthquakes and their causes as well as of their effects. Almost all estimation of seismicity is probabilistic and the probabilities may be computed from observed occurrences of earthquakes. Yet the length of time covered by seismological data is negligibly short when compared with the geological time scale involved in the seismicity of a region. In a given sample period, small events are more numerous than large earthquakes, which are important but rare events, and are not easily counted unless the period of observation is large. Thus, in spite of the considerable volume of data for earthquakes in the present century, a much longer period of observation is needed to permit a meaningful statistical treatment. This can only be achieved by resorting to data for earthquakes before 1900 and by choosing for study seismic regions which have a long and well recorded history.

The region selected for study is shown in Fig. 1; it comprises the Eastern Mediterranean basin which has a very long and well documented history. Initially, the work was based on a number of earthquake catalogues and other modern works dealing with earthquakes before 1900. But after checking a number of suspect entries against the original authority quoted, I found that in general these catalogues were unreliable. Additional checking proved that entries were based on comparatively modern works and on early sources of information at third hand¹. Apparently, seismologists who have often had to use literary sources at second hand have not been able to study early accounts critically. Thus, on many occasions, the same event, being described differently by various sources, was entered in their catalogues as two or even more events. Most of these catalogues have been copied by others without checking the mistakes, which are now being repeated in increasing numbers from publication to publication.

Thus, after experience of the difficulties caused by accepting the wrong data of modern writers, I decided to make a fresh collection of data based on contemporary evidence alone, with earthquake events set forth in an account of the local history

and geography, starting with the first century AD, and avoiding the use of modern works.

Basic data were first drawn from the Teubner Series (3.5%)* as well as from the *Patrologia Graeco-Latina* (10.5%), and these were supplemented by information extracted from the *Corpus Scriptorum Historiae Byzantinae* (6.0%). Information from these sources provided a broad basis for the study of events before the sixteenth century. This information was augmented and cross-checked with data in the special publications of a considerable number of early writers (16.0%), bringing the period of observation up to AD 1700. At this stage, a number of problems arose in connexion with the dating of certain events, and also with the location of a considerable number of the sites mentioned in early documents. For the period between the sixth and fourteenth centuries, Syriac sources (2.5%) not only added new material but also resolved some of the chronological ambiguities. The use of contemporary Arabic sources (22.0%) also added a very substantial amount of fresh information, particularly for the period between the ninth and the seventeenth centuries, and helped disentangle some of the dating and siting problems; they did create, however, new difficulties in chronology, some of which were resolved using both Armenian and, to a lesser extent, Georgian sources (8.5%). The most invaluable sources of information were found in manuscripts (14.0%), particularly in the form of marginal notes and colophons. For the most part these are eye witness or contemporary accounts usually providing accurate dates or reliable information from which the actual dates could be derived; they describe events in remote areas, usually in monasteries far from large centres of culture, thus supplementing information from better known chronicles. For the whole period studied so far, inscriptions (1.0%) and a very small number of coins were found useful not only for dating events but also for assessing the degree and extent of damage caused by a particular earthquake; public assistance and private generosity are usually recorded. The issue of new coinage and the establishment of new mints were often measures taken by early authorities to relieve regions after destructive earthquakes. Archaeological evidence from recent excavations was also helpful, particularly in regions for which written evidence is either inconclusive or scarce.

Of the earthquake events identified in the course of the past ten years of the present work, most have been found in my own perusal of the original documents, which is still far from complete. The material available at present, however, is coherent enough to permit some conclusions to be drawn about the historical and scientific value of earthquake records for the first sixteen centuries AD.

The total number of all earthquakes, large and small, identified so far for the period AD 10 to 1699, is just over 3,000, or about twenty times the number of genuine earthquakes listed for the same period in modern catalogues.

* Percentage of the total number of original sources.

Because of serious gaps in recorded history of the Greek mainland, Macedonia and Albania, the homogeneity of the data for this area is relatively low. For the area east of the fortieth meridian, including the Red Sea, and for the period before the seventh century, the homogeneity of the data is even lower. For the rest of the region the sources of information are uniformly distributed in space and time and for the larger shocks, about 2,200 in all, the homogeneity of the material can be proved to be satisfactory for the whole period.

earthquake in AD 17 which affected the region recently damaged by a destructive earthquake on April 2, 1968. The earthquake of AD 17 destroyed twelve cities along the river Gediz, from the Aegean coast to Alashehir (Fig. 2). The earthquake happened at night and the destruction it caused was aggravated by conflagration. As a result of the earthquake certain parts of the Gediz valley were uplifted and others, sank, the ground opened up in places and large landslides added to the damage. This earthquake is mentioned by Strabo (xii, 8; xiii, 3/4) who names

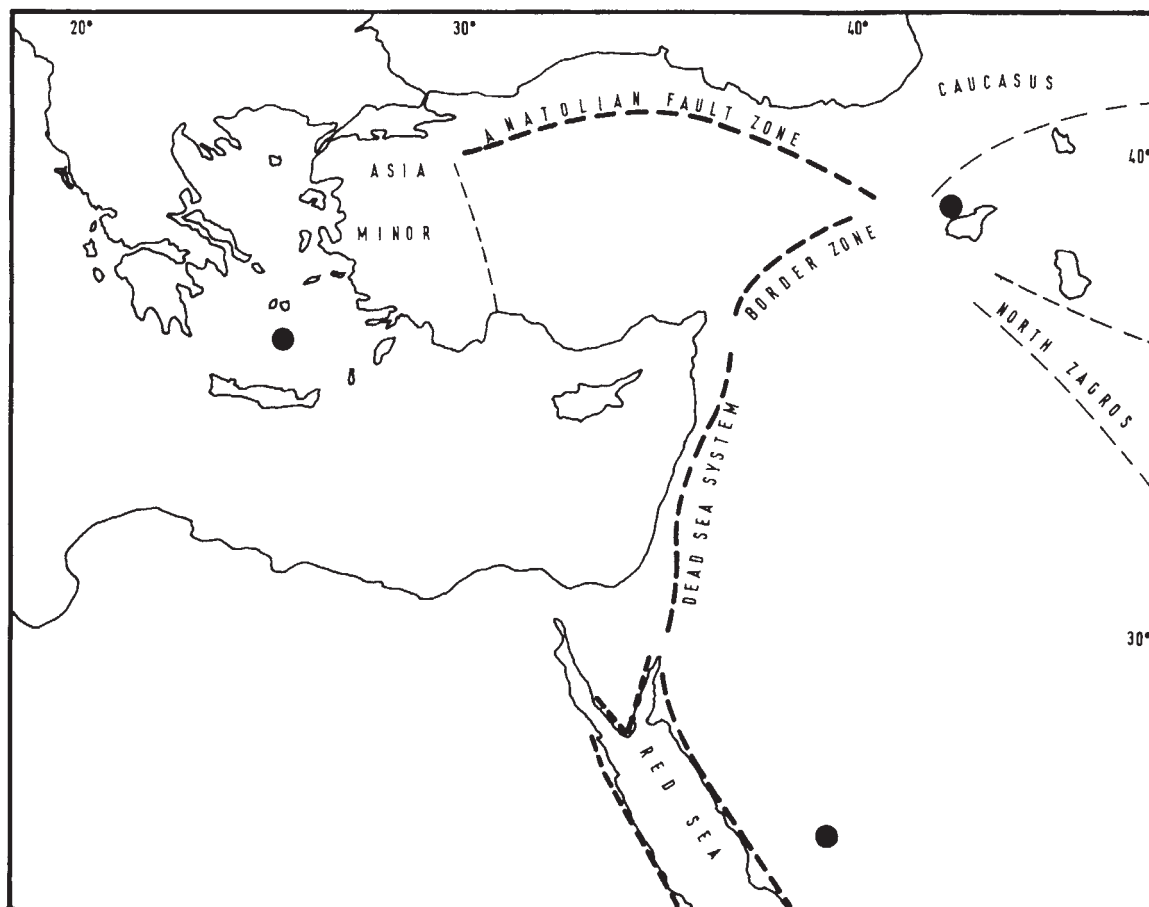


Fig. 1 The area of study.

It is often argued that it is the largest and most populous centres of culture that furnish most of the data about early earthquakes and that historical seismicity usually seems to be concentrated around large cities. This apparent concentration of seismicity is the result of the scanty and often inaccurate information given in modern earthquake catalogues. Modern writers seem to have been unable to study original sources critically or to identify localities affected by early earthquakes other than obvious ones. Thus, an unmodified use of the data in modern catalogues would lead to the absurd conclusion that the most seismic areas in the Middle and Near East are Istanbul, Antakya, Aleppo, and Jerusalem. But earthquakes felt in and reported from large cities originated in most cases from epicentral regions 50 to 400 km away where they caused heavy damage, accounts of which have been found either in less well known chronicles or in marginal notes, colophons and inscriptions written in remote areas which for centuries remained unaffected by significant population movements or by changes in the density of population.

The method used for the study of early events can best be illustrated by summarizing a typical example, that of the

only Magnesia and Sardis. Tacitus (ii, 47) gives more information about the twelve cities destroyed, which he names as Myrina, Aegae, Kyme, Temnus, Apollonis, Hyrkanis, Hierocaesarea, Mostene, Temnos, and Philadelphia. Pliny (n.h. ii, 200) and Seneca (n.q. vi, 1) call this earthquake a major disaster and give twelve as the number of the cities destroyed. Dio (l vii, 17) attests the dispatch to Asia Minor of a senatorial commissioner with five lictors charged with the relief of the area as well as the remittance of large sums of money for reconstruction. Eusebius (2032) places this event in a.A. 2032, commencing October AD 16 and also in the third year of Tiberius, which are consistent with AD 17, but adds to the destroyed cities Dia and Ephesus. Hieronymus (566) adds Ephesus and Dia, but dates the event in the fifth year of Tiberius which is at least one year too high. *Chronicon Pseudo-Dionys* 93 gives the same date but adds only Ephesus. Later writers follow either Eusebius or Hieronymus, and some of them omit Kyme. Most of the earlier sources, Prosper (372), Dion. Telmar (46), Syncelus (319/603), record this earthquake in a.A. 2032, ending in October AD 17. Eusebius as well as Hieronymus add to the list a fourteenth city, Dia, which they

do not count, however, and which is not mentioned in the Puteoli inscription. This inscription was found at Puteoli and bears the names of the twelve cities destroyed by the earthquake as well as that of Ephesus (CIL x, 1624). As this monument was set up in AD 30, twelve years after the earthquake, it is almost certain that Ephesus may have suffered and been relieved at a later date than the rest. In AD 22 a monument was erected in Rome by the restored cities in gratitude to Tiberius (BMC. Emp. i, Tib, 70); this monument is also described by Phlegon (42) and it refers to the twelve cities excluding Ephesus. It seems very likely that Dia has been derived

from the dative case of Apollonis through an oversight of a later copyist of Eusebius's work (dat. Apollonidia = Apollonia-Dia). As Dia is found in texts always following the word Apollonis, or as in the Puteoli inscription the two names are joined together giving Apollonidea, we may assume that Dia did not suffer from the AD 17 earthquake. It must be pointed out, however, that Dia is given as a separate city damaged by this earthquake in Stephanus of Byzantium, who places it in Caria; perhaps Stephanus confused Dios Hieron, which is situated a few kilometres north of Ephesus in Lydia, with the alleged city of Dia. Sardis and Magnesia were almost totally destroyed

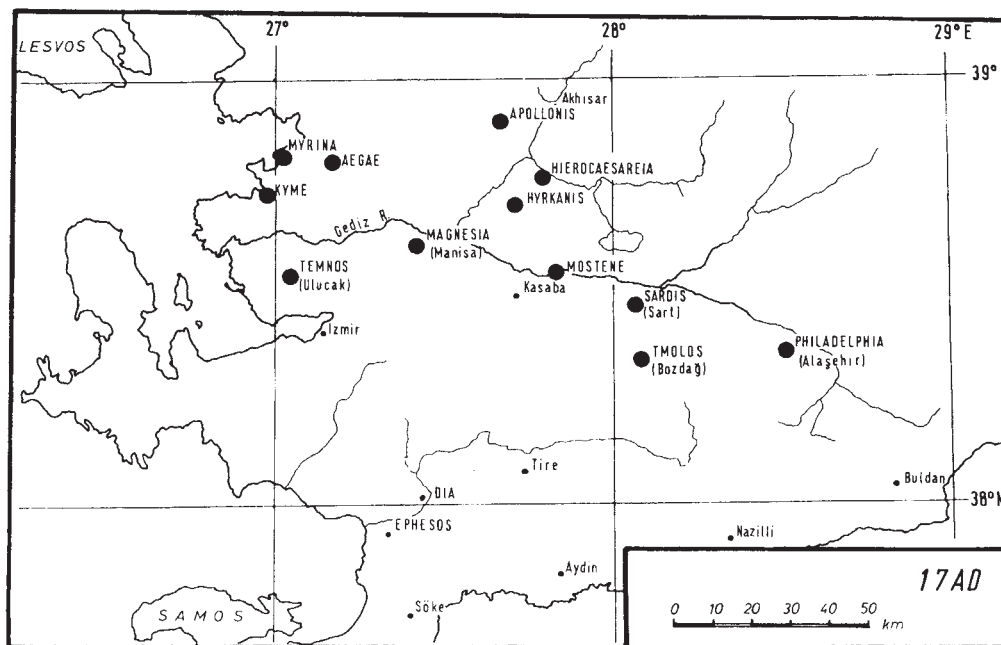


Fig. 2 Area affected by the earthquake of AD 17.

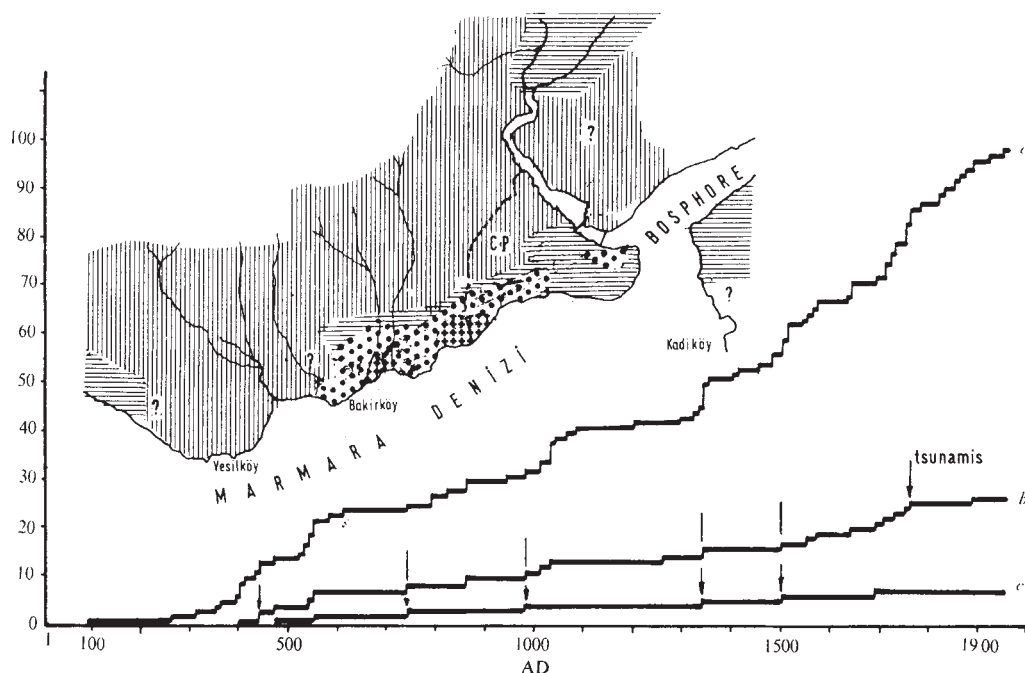


Fig. 3 Seismic activity in the Istanbul region.

and received considerable financial assistance from Rome as well as remission of all contributions to the Imperial Exchequer for a period of five years. Remission of tribute to the public exchequer for the same period was given to the other ten cities, *Res Gestae divi Augusti*. Sardis was rebuilt on an extensive plan. Recent excavations show an unusual type of foundation construction used in the reconstruction of the part of the city on the east bank of the Paktolos river—a grid of wooden beams under the foundation on which the structure was built. All evidence shows that this was a major earthquake.

From the study of individual events, in a manner similar to that given above, the seismicity of a particular area may be investigated over a long period of time. A typical though not

quiescence are again noticeable, but also groups of strong earthquakes, marking distinct increases in seismicity, with an average rate of about one damaging earthquake every 55 years. Finally, Fig. 3 (curve *c*) shows the distribution of destructive earthquakes that ruined large parts of the country around Istanbul, causing heavy damage with large numbers of casualties in the city itself. Some of these shocks were followed by comparatively short periods of high seismicity which often occurred near the end of long periods of relative quiescence; most of these large shocks were associated with seismic sea-waves, some of which were of catastrophic magnitude.

Frequency curves, similar to those shown in Fig. 3, have been prepared and studied for a number of regions. They show that

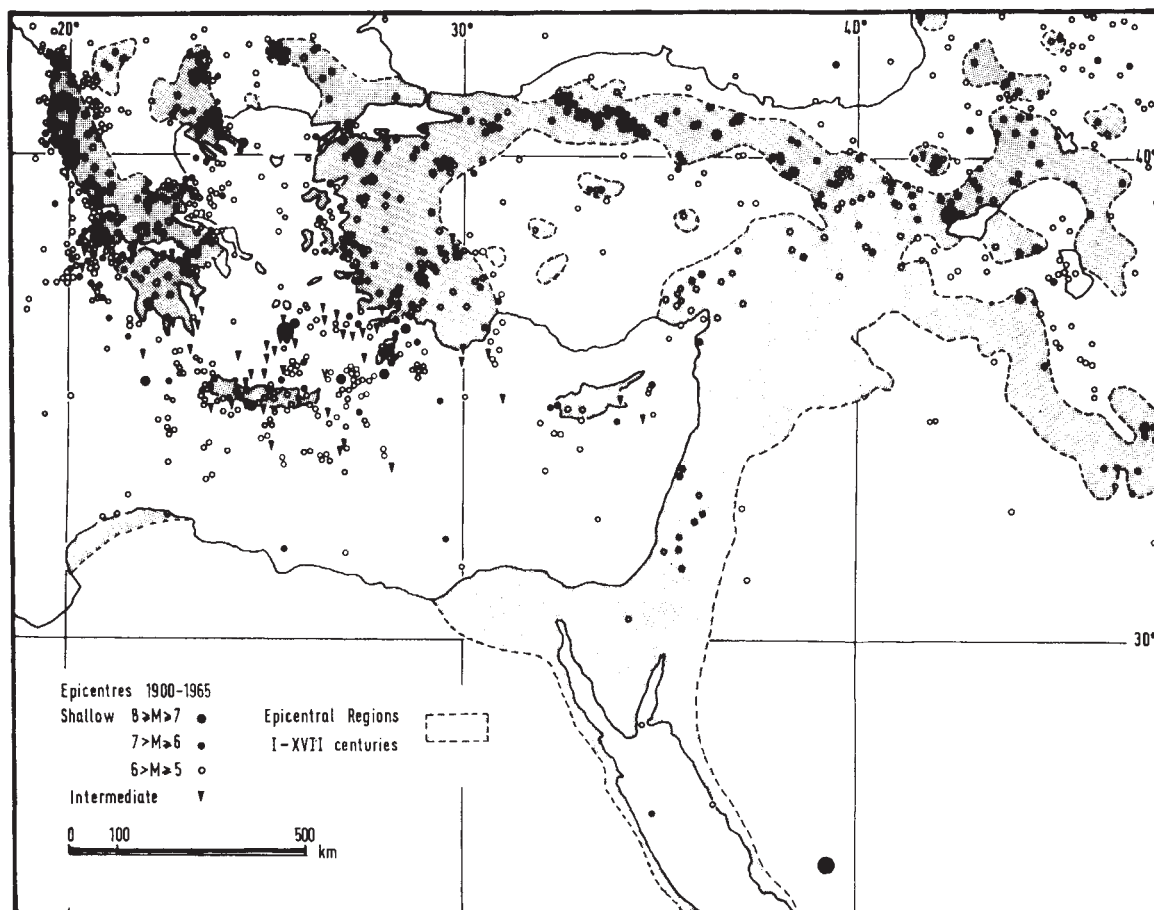


Fig. 4 Distribution of historical seismicity.

the best example of early seismicity is that for the region of Istanbul. Fig. 3 (curve *a*) shows the time distribution of all strong earthquakes that caused alarm and also some damage in the city. There are two conspicuous periods of relative quiescence, and about 200 years long, centring on the seventh and twelfth centuries respectively. These are periods of genuine inactivity and are not due to lack of information. Indeed, the second of these periods coincides with the period of the Crusades for which we have the largest amount of information from occidental sources. From the same figure we notice that the frequency of occurrence of strong earthquakes in the fifth and sixth centuries is the same as that for the period after the fifteenth century. Fig. 3 (curve *b*) shows a similar plot for shocks that caused widespread concern over a large area and also considerable damage in Istanbul. Long periods of

earthquake frequency is subject to marked fluctuations rather than to any general monotonic variation. They show also that the data available for the seventeen centuries are sufficient for the detection of secular changes in local seismicity but inadequate to establish whether these changes are subject to a law. It is my impression that historical data are useful for the study of continental tectonics, of the migration of seismic activity in contiguous tectonic units as well as of the interaction between such units. For prediction purposes, however, a much longer period of observations is needed, for which no foreseeable means of data gathering seems likely.

The distribution of historical seismicity is shown by the shaded areas in Fig. 4. This map was constructed by superimposing all epicentral areas of individual earthquakes such as the one shown in Fig. 2. The map shows quite clearly that

historical seismicity follows not only a well defined pattern but also that this pattern fits surprisingly well to boundaries of major tectonic units (Fig. 1). Thus the Red and the Dead Sea Systems, the broad Border Zone and its contact with the Anatolian Fault Zone and North Zagros, are very well defined. Complex zones in Greece and in western Asia Minor are less clearly depicted.

Instrumental data for the past 65 years, shown on the same figure, fit the pattern of early seismicity equally well. There is, however, a noticeable lack of instrumental data in the Border Zone, in the Zagros and in the Red and Dead Sea systems, which is obviously due to the relative quiescence of these regions during the present century. Consequently, it would seem that in certain cases of continental tectonics the formulation of theories on the basis of instrumental data alone, without due consideration of the time-scale involved in certain seismic processes, is bound to lead to erroneous or incomplete results.

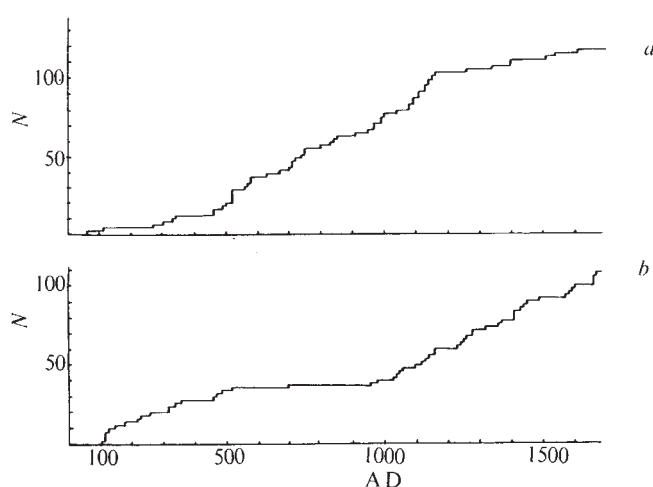


Fig. 5 Time distribution of damaging earthquakes. *a*, Border Zone; *b*, Anatolian Zone. *N*, Number of damaging earthquakes.

The study of interaction and migration of seismic activity in contiguous tectonic units is interesting. Fig. 5 shows the time distribution of damaging earthquakes (*a*) in the border zone and (*b*) in the Anatolian Fault Zone, the two units being contiguous. From this figure it is clear that during the first five centuries the Border Zone was comparatively quiescent while the Anatolian Zone was active. During the following six centuries the pattern was reversed, only to be reversed again during the eleventh century with a few centuries of overlapping activity. A similar cyclic pattern, but with longer periods of overlapping activity, was noticed for the Border Zone and the Dead Sea System. At this stage, however, a more detailed study of the interaction and correlation of activity of contiguous units is not warranted.

Faced with a high degree of uncertainty, but pressed by the requirements of a technical society for judgment and decisions, seismologists, geologists and engineers make daily estimates of seismicity with varying degrees of success. The study of historical earthquakes brings out two important points that should be taken into consideration when early events are used in seismicity assessments.

The first point concerns the interpretation of early earthquakes. To each of the curves shown in Fig. 3, or to any other frequency curve, corresponds a particular intensity, the precise value of which cannot be assessed. The reason for this is that intensity, being a measure of the effect of a particular earthquake on man-made structures, cannot properly be used to

relate early and modern events. Modern buildings differ in many respects from old ones and to judge future damage from century old case histories can be seriously misleading. For instance, the exact repetition of an old earthquake at the present day will differ not only in the types of structures damaged but also in the degree of damage. In some cases modern structures will be more severely damaged than old buildings. A distant large earthquake ten centuries ago would have caused practically no damage in Istanbul, Ankara or Jerusalem; the same earthquake today would cause damage to a large number of long-period structures in these cities.

The second point concerns the assessment of seismicity using extant structures of old age. It is usually considered rather improbable that early structures, liable to damage by earthquakes, could stand for many centuries in seismic regions. The mere fact that quite a few early monuments are still to be found in a state of tolerable preservation in various parts of the world has led to the belief that these parts should be free from destructive earthquakes². But historical and archaeological evidence shows that this is not the case. The early buildings that are still standing have in fact, during their lifetime, been subjected to a number of destructive earthquakes, and they have survived through a process of natural selection. They are a very small fraction of the total number of structures that existed in early times and they represent a sample of structures of the best final design and construction, achieved through the ages by a trial-and-error technique or by chance. Furthermore, frequent references occur in early literature to extensive repairs of walls, churches and other buildings, because of earthquake damage, where the occasion was taken to introduce changes in the design and construction which produced a more resistant structure. Thus, the mere fact that a few early monuments are still standing in various sites in Greece, Turkey, Iran or even in Skopje and in Istanbul, should not be taken to mean that these sites have been free from damaging earthquakes.

Perhaps it is one of our most interesting findings that the lasting effects of major earthquakes during the past twenty-five centuries would not seem to have been very significant. Soon after a large earthquake, vested interests invariably led people to act once again with disregard for the prospect of further such calamities. Yet modern writers^{3,4} have attempted to use earthquakes to account for gaps in the sequence of civilizations and for movements of peoples, hypotheses for which I can find absolutely no historical justification. Earthquakes in the past twenty-five centuries have had little, if any, serious influence on historical developments in the Middle and Near East. They did often account for the premature decline of a local economy or for a crisis in local human affairs. But they have never caused the ruin of a culturally advanced state, far less the end of a civilization. In contrast with wars, epidemics and other long lasting calamities which have serious and prolonged effects, earthquakes, no matter how large, seem to have had little long-term impact on Man. It may be that men react to the inevitable hazard in a special way, distinct from the preventable hazards⁵. Personal, political and economic interests seem to overshadow, and in some cases suppress, the lessons to be learnt from destructive earthquakes. For example, villages ruined by early earthquakes are often rebuilt on different sites, whereas cities, where significant economic and political interests were involved, have been rebuilt, enlarged and embellished, invariably on the same site, even when it was known that the site was unsuitable and that it had contributed to the magnitude of the disaster.

This work, which began early in 1960 and which is still in progress, has been supported by UNESCO (1969–71).

¹ Sieberg, A., in Gutenberg, B., *Handbuch der Geophysik*, 4, *Denkschr. Mediz.-Naturw. Gesellsch.*, Jena, 2 (1932).

² Frech, F., *Z. Gesellsch. Erdkund.* Berlin, 576 (1915).

³ Marinatos, S., *Antiquity*, 3, 425 (1939).

⁴ Schaeffer, C. F., *Stratigraphie compare et chronologie de l'Asie Occidentale pour les I^{le} et II^e millénaires* (Oxford, 1948).

⁵ Burton, I., and Kates, R., *National Resources J.*, No. 3 (1964).

Discovery of Postcranial Remains of *Homo erectus* and Associated Artefacts in Bed IV at Olduvai Gorge, Tanzania

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The discovery of a left femur shaft and hip bone of *Homo erectus* in association with an Acheulean industry in Bed IV represents the first direct association at Olduvai of a well defined artefact assemblage with *H. erectus*.

THE shaft of a left femur and a pelvic fragment attributed to *Homo erectus* (Olduvai Hominid 28) that are described by Dr M. H. Day in the following article¹ were found *in situ* during excavations in 1970 at site WK (Wayland's Korongo),

Olduvai Gorge. This site lies on the south side of the gorge, 1.25 miles below the junction of the main and side gorges. Hand axes and cleavers had first been observed there on the scree below Bed IV during 1932, but no excavations were undertaken before 1970, when a systematic exploration of Bed IV was carried out.

The two hominid bones were found on a well defined surface and lay 1.5 m apart, with the anterior aspect of the femur shaft and the interior or pelvic aspect of the innominate bone upwards. Several artefacts and broken remains of fauna lay nearby (Fig. 1). Subsequent excavations, during which approximately 18 × 10 m were cleared down to the level of the hominid bones, revealed that they were on the higher part of an uneven, eroded surface which could be traced over the whole of the exposed area. To the south-west, the surface dipped down into

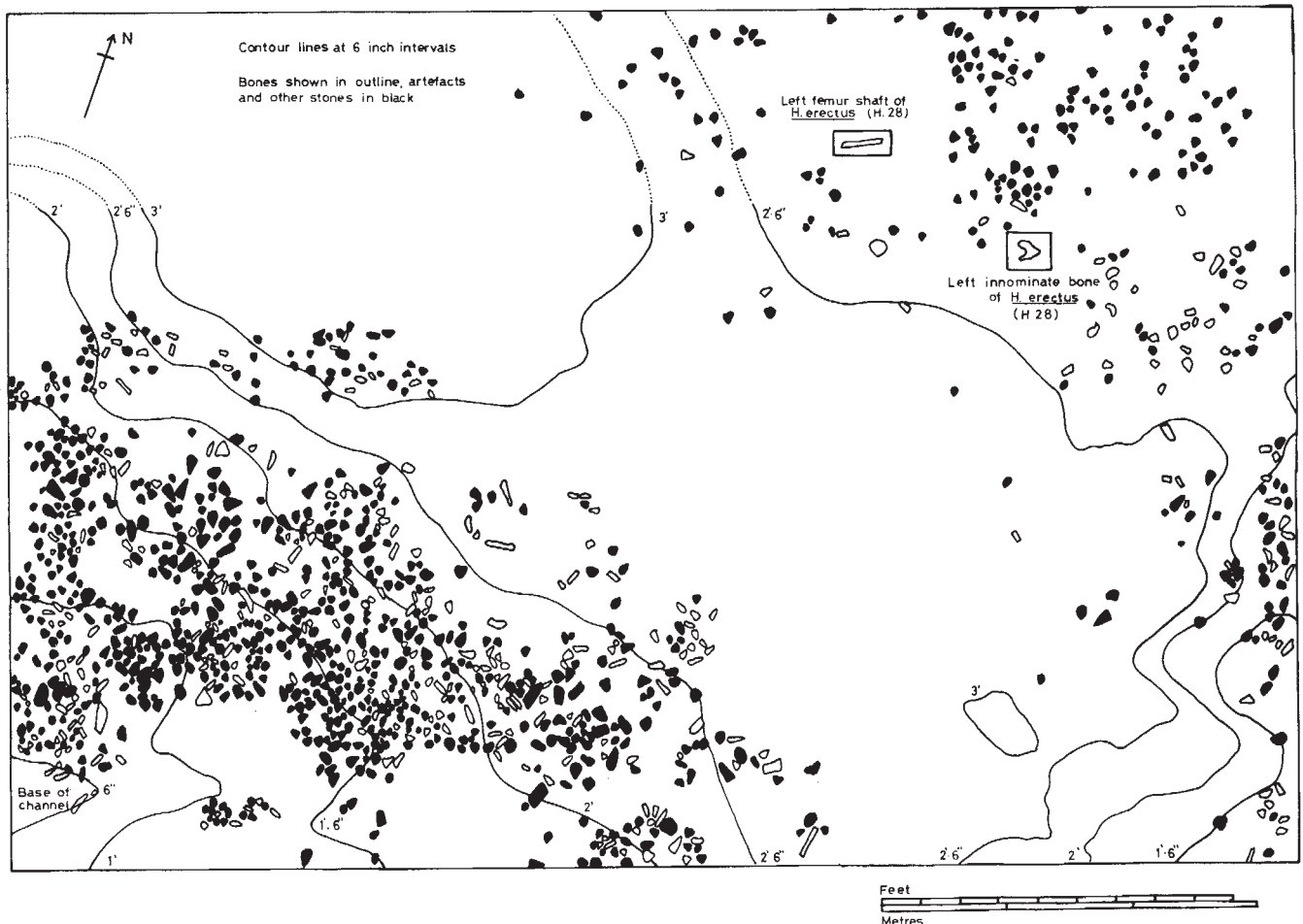


Fig. 1 Association of artefacts and *H. erectus* remains at site WK. Contour lines are at 6 inch intervals. Bones are shown in outline; artefacts and other stones are shown in black.

a channel approximately 1 m deep that was aligned roughly NE-SW. Several irregular depressions were uncovered in the eastern part of the area, none of which exceeded 0.75 m in depth; the bases of these depressions and of small hollows in the principal channel were clearly marked by a thin coating of silt.

Both the principal channel and the depressions contained dense accumulations of occupational debris, incorporated in a coarse sandy matrix. This level yielded a total of 2,600 specimens comprising hand axes, cleavers and other artefacts, including artificially pitted stones, faunal remains and unmodified cobbles. Abrasion is evident on some of the specimens but many are sharp and do not seem to have been weathered or transported by water for any considerable distance.

Two more horizons containing artefacts were uncovered at this site, the lowest in a conglomerate at the junction of Beds III-IV and the second approximately 1 m below the hominid level (Fig. 2).

Geology of the Site

Dr R. L. Hay of the Department of Geology, University of California, Berkeley, whose monograph on the geology of Olduvai Gorge is now in preparation, has supplied the following note on the geology of the site, with the accompanying section (Fig. 3).

Bed IV ranges from 20-22 feet thick in the vicinity of WK. It sharply overlies Bed III and is overlain by aeolian tuffs of the Mesak Beds (formerly known as Bed IVb). Bed IV is 50%-60% claystone and most of the remainder is sandstone and conglomerate, which form lenticular beds. The claystones are usually sandy, root-marked, and locally contain vertical veins of sandy claystone a centimetre thick and a few feet long that represent deep mud cracks filled by sediments during the deposition of Bed IV. Most sandstones contain both volcanic and quartzose basement debris.

A marker tuff (Tuff IVb) extends through most of this area near the middle of Bed IV. It is as much as 7 feet thick, hard and reddish-brown, and is characterized by altered mafic glass and abundant rock fragments. Most of the tuff is thin-bedded or laminated. The tuff is locally eroded away and fragments of it occur in the lowermost sandstones and conglomerates above the tuff. The hominid fossils were found at the base of a sand-



Fig. 2 Artefacts and other stones in the channel at site WK. A pitted cobble can be seen below the scale.

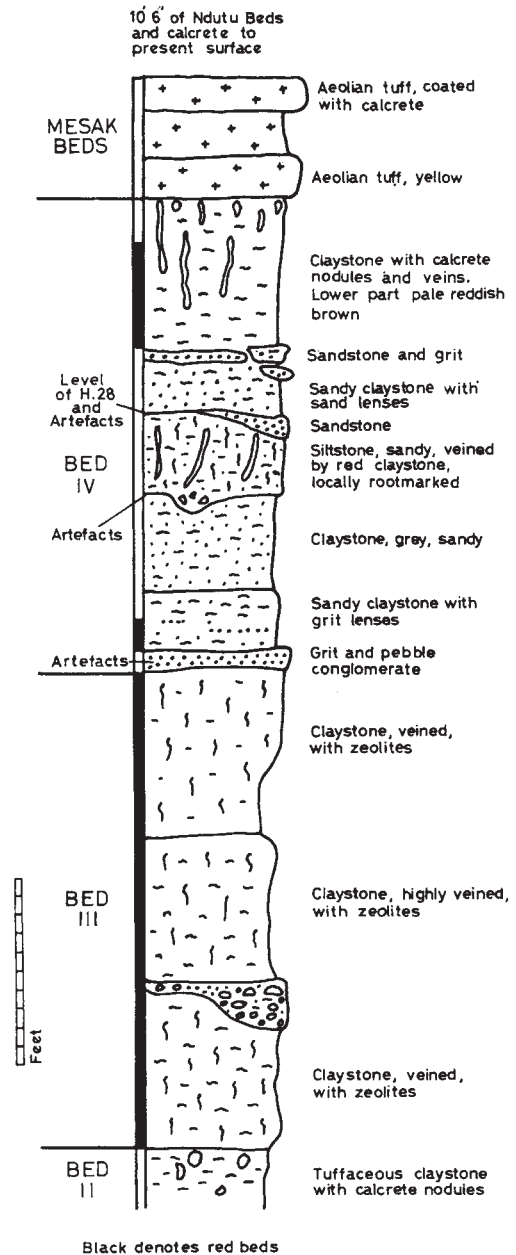


Fig. 3 Stratigraphic section of site WK prepared by R. L. Hay. Black denotes red beds.

stone with fragments of the tuff, showing that they postdate the tuff, but probably by only a short period of time.

The non-tuffaceous deposits of Bed IV are fluvial; sandstones and conglomerates fill the stream channels, and the claystones represent overbank deposits. The WK area lay near the drainage axis of the Bed IV basin which received volcanic detritus from the south and east, and basement detritus from the north and west. Tuff IVb was deposited in a temporary, small, saline playa lake, at a time when the climate was relatively hot and dry.

Recent geomagnetic polarity measurements on red beds provide a basis for tentatively estimating the age of Bed IV. A. Brock (University of Nairobi) has found reversed polarity in three samples from the upper part of Bed II and one from upper Bed III; a sample from near the base of Bed IV is normal. These few data, added to data from Bed I and the lower part of Bed II², suggest that the boundary between the Matuyama Reversed and Brunhes Normal epochs, dated at about 0.7 m.y.², lies approximately at the base of Bed IV. The Lemuta (= aeolian tuff) Member of lower Bed II has an age of about 1.65 m.y.³. Extrapolating on the basis of stratal thickness between the

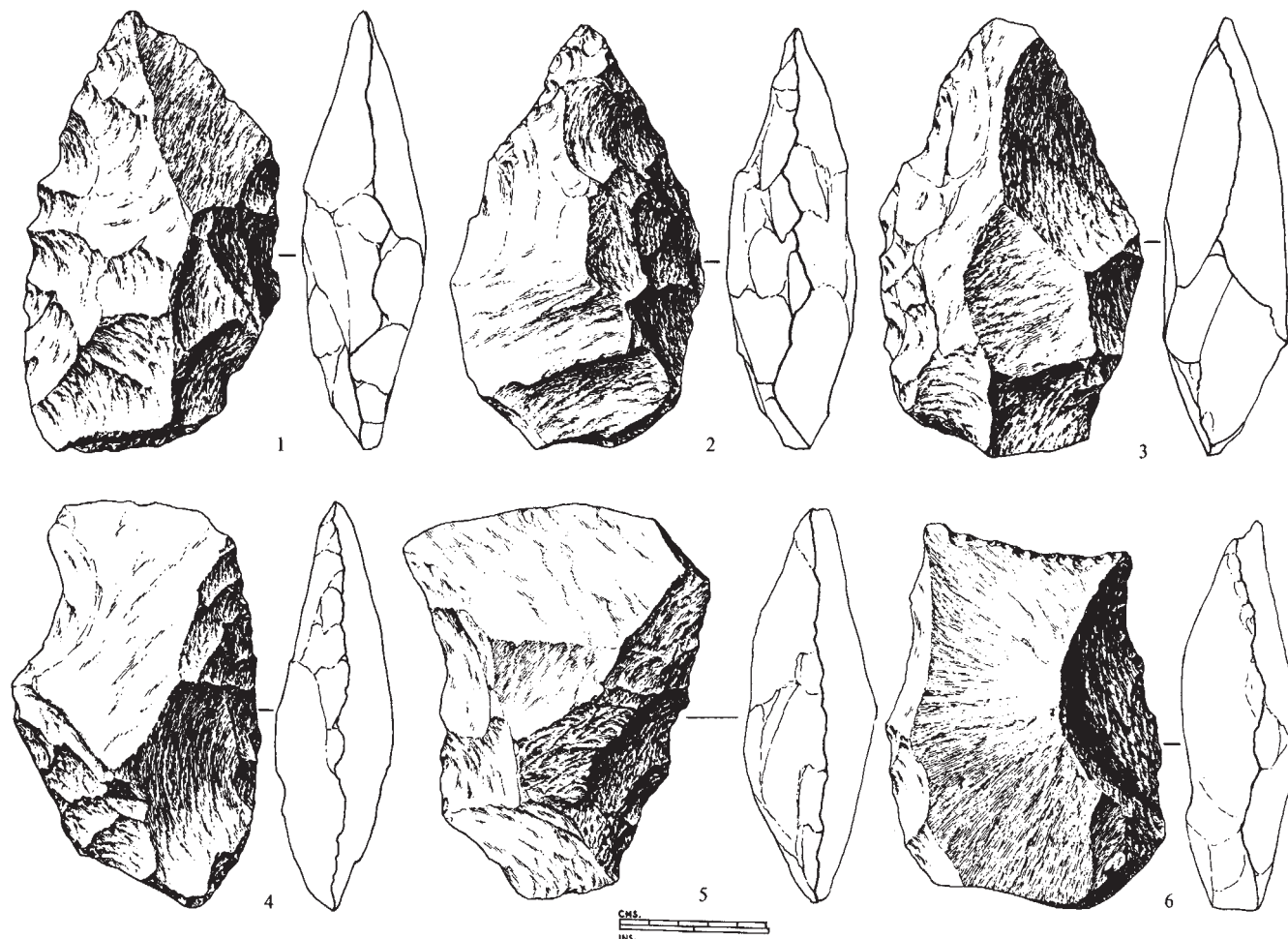


Fig. 4 Hand axes (1-3) and cleavers (4-6) associated with the *H. erectus* remains.

levels of 1.65 and 0.7 m.y., the top of Bed IV may be about 0.3 or 0.4 m.y. old, and the hominid fossils may have an age of about 0.5 m.y.

Artefacts

The sample of occupational debris reviewed here consists of 494 artefacts (Table 1), 347 unmodified cobbles and 257 largely fragmented remains of fauna. This material was obtained from one trench within the principal channel and can be considered to represent a fair sample from the hominid level.

Table 1 Artefacts recovered from Site WK

Tools	Nos.	%
Hand axes	20	15.9
Cleavers	23	18.2
Bifacial tools, broken and unfinished	7	5.5
Choppers	11	8.7
Discoids	9	7.1
Spheroids	10	8.0
Scrapers, heavy and light duty	24	19.0
Small tools, various	22	17.5
Utilized material		
Pitted cobbles	41	35.6
Cobbles, battered	20	17.4
Miscellaneous	50	43.5
Hammerstones	4	3.5
Debitage	253	

Most of the hand axes and cleavers have been made on side or end struck flakes, the former predominating. They are mostly of trachyandesite, though there are a few examples of phonolite

and tabular quartzite. The striking platforms have been only roughly trimmed off and one face usually consists almost entirely of the untrimmed primary flake surface. With few exceptions these tools show a minimum degree of retouch and most of the trimming scars are large and deep. Only two specimens, both made from fine grained phonolite, exhibit some "resolved" flaking. The average number of trimming scars is low: 10.5 per specimen in both hand axes and cleavers, a figure that compares closely with that for the Early Acheulean hand axes from Middle Bed II⁴. The hand axes are roughly ovate in form but are markedly irregular. In the cleavers, square or oblique ended examples predominate and chisel ended specimens are rare. In spite of their general crude appearance, both hand axes and cleavers are more or less the same size and have similar breadth/length and thickness/length ratios; it is clear that they represent a homogeneous series (Table 2).

The forty-one pitted cobbles are a prominent feature of this industry and they also occur at other sites nearby of approximately the same stratigraphic level. These stones range in size from specimens no more than 5 cm in diameter to small boulders weighing several kilograms. The pits or hollows are also variable in size and measure from 1 to 5 cm in diameter. They sometimes occur singly, but are more often in pairs, one on either side of a stone; some examples have up to six hollows.

Table 2 Average Measurements of Hand Axes and Cleavers

	Length (mm)	Breadth (mm)	Thickness (mm)	Breadth/length ratio (%)	Thickness/length ratio (%)
Hand axes	142	84	41	61.3	28.9
Cleavers	133	90	45	67.5	34.2

Among the unspecified small tools are a number of thick-set quartz points, triangular or quadrilateral in cross-section, that are usually heavily utilized at the tips. These tools also occur at other sites where there are pitted cobbles and it seems possible that they were used in conjunction with the cobbles, perhaps as punches.

Artefact assemblages from three sites excavated within 1–2 km of WK, that are virtually contemporaneous with the hominid level, have still to be studied in detail, but it is clear that they are at variance with the WK industry in a number of important respects, particularly in the proportionately small numbers of hand axes, total absence of cleavers and relative abundance and variety of small tools. Large side and end struck flakes do not occur and the rare hand axes are made on small “cores” flaked over both faces. It is evident that the technique of biface manufacture was fundamentally different, although the materials used are the same and are also known to have been obtained from the same sources.

To conclude, the industry from the hominid level can be referred to the Acheulean in view of the proportionately high number of bifacial tools (39.6%), among which cleavers are unusually common. The hand axes bear strong resemblances to

the Early Acheulean series from EF–HR in Middle Bed II, to which they seem closer than to contemporary series excavated from Bed IV.

Although other human remains that may be attributed provisionally to *Homo erectus* have been found at Olduvai, in upper Bed II⁵ and in Beds III–IV⁶, where abundant artefacts also occur, the discoveries at WK are the first occasion on which a well represented lithic industry has been directly associated. It is not certain whether this association implies that *H. erectus* was responsible for the industry, but it seems likely, because there are other lines of evidence at Olduvai suggesting a link between the Early Acheulean of Bed II and *Homo erectus*⁴.

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¹ Day, M. H., *Nature*, **232**, 383 (1971).

² Grommé, C. S., and Hay, R. L., *Earth Planet. Sci. Lett.*, **10**, 179 (1971).

³ Cox, A., *Science*, **163**, 237 (1969).

⁴ Leakey, M. D., *Olduvai Gorge*, **3** (Cambridge University Press, in the press).

⁵ Leakey, L. S. B., and Leakey, M. D., *Nature*, **202**, 3 (1964).

⁶ Leakey, M. D., *Nature*, **223**, 754 (1969).

Postcranial Remains of *Homo erectus* from Bed IV, Olduvai Gorge, Tanzania

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Anatomically, the postcranial remains of Olduvai Hominid 28 seem to have a close resemblance to the *Homo erectus* material from Choukoutien.

THE discovery of postcranial fragments of Olduvai Hominid 28 reported by Mrs Mary Leakey in the previous article¹ is of great interest because the bones throw some light on the structure and function of the lower limb skeleton of Middle Pleistocene hominines in East Africa. The only lower limb material of a hominine of this approximate age known previously consists of the femora from Choukoutien, China, and the femora claimed to be of this age from Trinil, Java.

The first Trinil femur (Femur I) was recovered by Dubois² and his workers allegedly from the same horizon as the calotte of “*Pithecanthropus*” *erectus* (Dubois, 1894)≡*Homo erectus* *erectus* (Campbell, 1964). At the turn of the century, the association of this femur with the calotte was strongly questioned, and often subsequently, on the grounds that its modern features are at variance with the more primitive features of the calotte. When Weidenreich later described³ the Choukoutien remains of “*Sinanthropus pekinensis*” (Black, 1927)≡*Homo erectus pekinensis* (Campbell, 1964), he would not accept that the Trinil femur should have been attributed to “*Pithecanthropus*” and stated that it “. . . must be attributed to a type more closely related to modern man” because it differed so markedly from the Choukoutien femora. Nevertheless, it has been widely assumed for 30 yr that the Trinil femur was good evidence that the lower limb of *Homo erectus*,

and by inference the remainder of the postcranial skeleton, was fully evolved and virtually of *sapiens* type by the Middle Pleistocene in Java; it was thus assumed that the subsequent evolution of *Homo* was confined almost entirely to the cranium, jaws, teeth and brain.

The discovery of new femoral and pelvic material in East Africa, in a well documented layer associated with artefacts, casts serious doubts on this assumption.

The Femur

The femur is represented by most of the shaft; it lacks the head and the greater trochanter. Parts of the neck and the lesser trochanter are preserved but the shaft is broken off just above the popliteal surface (Figs. 1 and 2).

The shaft is flattened throughout its length with acute medial and lateral borders. The flattening (platymeria) of the upper end is exaggerated by the presence of a marked lateral expansion at the level of the gluteal tuberosity. The lower end of the shaft is just beginning to expand for the condyles at the point of breakage, and the upper end shows the beginning of the lateral expansion for the neck and the postero-medial expansion for the base of the lesser trochanter.

The medial border of the shaft is convex along its length and the narrowest point on the shaft (medial to lateral) is very near to the distal end. Laterally, the shaft is gently convex antero-posteriorly and gradually expands from the subtrochanteric region to the point of shaft breakage below. From the front the shaft is straight.

The muscular impressions on the bone are remarkably clear, particularly the direct attachment of the gluteus maximus which is a combination of a crista hypotrochanterica and a fossa hypotrochanterica. The third trochanter is not preserved, if it was present, but it is possible that there was a

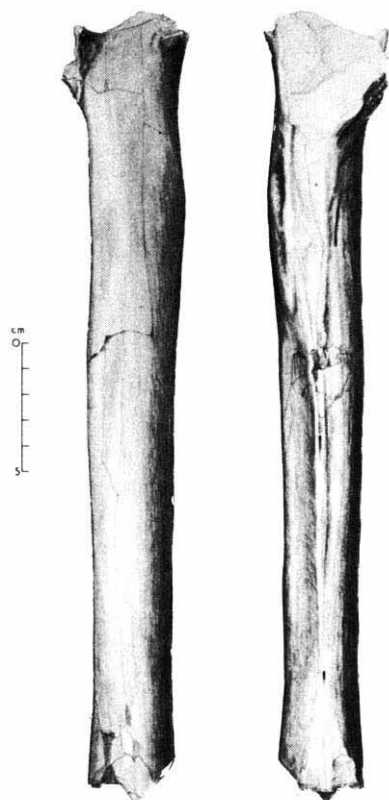


Fig. 1 Femoral shaft of Olduvai Hominid 28, anterior and posterior views. (Drawn by Audrey Besterman.)

tubercle at the top of the hypotrochanteric crest, a feature that continues up to the base of the greater trochanter.

At the upper end of the bone the spiral line is present for the attachment of vastus medialis muscle as well as a weaker pectineal line for the attachment of pectineus muscle; these lines are separated by a roughened area for the anchorage of iliacus muscle. Between the spiral line and the gluteal crest the upward extension of the ridge for adductor magnus can be discerned.

The ligaments around the hip joint seem to have been powerful because the sharp corner at the upper medial extremity of the specimen is crossed by the intertrochanteric roughening for the iliofemoral ligament; similarly, the triangular attachment of the medial band of the pubofemoral ligament is easily identified.

The linea aspera is present and divides towards the lower end into diverging medial and lateral condylar lines; there is no pilaster. Above, the attachment of vastus lateralis curves away from the linea aspera towards the lateral side and skirts the gluteal tuberosity; this permits the upper fibres of the short head of biceps femoris to mark the bone as a short ridge between the linea aspera and the gluteal tuberosity. There are three nutrient foramina, all small and placed near to the linea aspera.

X-rays show a thinning of the cortex towards the lower end of the specimen and the medial and lateral trabecular systems of the neck and upper end are clearly apparent. It would be impossible to see Ward's triangle, even if it were present, because it would have been above the upper fracture line. The medullary cavity is of moderate calibre and is generally wider than deep; the cortical thickness is greater in the coronal plane than it is in the sagittal plane at the mid-shaft. The range of modern human variability of total medio-lateral cortical thickness at the mid-shaft is large⁴. Hominid 28 shows a total thickness of 16 mm medio-laterally and 11 mm antero-posteriorly at the same point. The inferior aspect of the neck shows a well marked cortical buttress that is still

8 mm thick at the point of breakage; this is considerably thicker than is common in modern man.

The Hip Bone

The hip bone (os coxa) is represented by the major parts of its iliac and ischial portions (Figs. 3 and 4); the pubic portion is missing. The ischium lacks the tip of its spine and the ischial portion of the ischiopubic ramus, and the ilium lacks the anterior superior iliac spine. The specimen shows several cracks most of which are not displaced, but over an area of the anterior part of the iliac fossa there is a little distortion, so that there is an irregular depression of the surface and some lateral displacement of the anterior one-third of the iliac flange. This displacement is confirmed by the presence of an open crack on the medial aspect of the upper part of the anterior inferior iliac spine. Viewed from in front the ilium is canted laterally, slightly accentuating the prominence of the iliac pillar. The posterior half of the dorsum ilii also displays some cortical cracking with minor displacements and depression of the surface of the bone. There are several tooth marks on the specimen. There is no evidence of bone pathology or of the generalized effects of systemic disease.

The bone is stoutly constructed with prominent muscular and ligamentous markings and a large acetabulum indicating a large femoral head. The articular surface of the acetabular fossa is smooth and the non-articular region is thin. The ischium is relatively small by comparison with the acetabulum and is separated from it by a deep and narrow groove. This groove seems to be accentuated by the medially rotated position

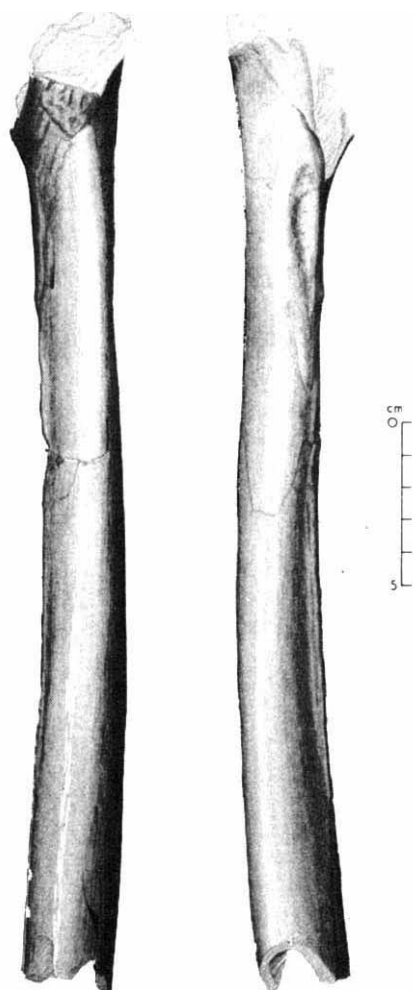


Fig. 2 Femoral shaft of Olduvai Hominid 28, lateral and medial views. (Drawn by Audrey Besterman.)

of the ischium. This also gives an appearance of shortness of the ischium that may not be fully borne out in reconstruction of the missing portion. The ischial tuberosity shows a well marked attachment for semimembranosus separated from that of the long head of biceps femoris and semitendinosus by the oblique ridge. On the lateral aspect of the ischial tuberosity the impression for quadratus femoris muscle can be seen, as well as some roughening for obturator externus muscle on the antero-lateral part of the ischial ramus. The medial surface of the ischium below the spine is smooth and rounded for the play of the tendon of obturator internus muscle.

The ilium is large and characterized by its prominent muscular markings and ligamentous impressions as well as the presence of an extremely robust vertical iliac pillar. Although it is true that this pillar may be slightly exaggerated by the distortion of the anterior part of the bone, none the less the feature is more prominent than on any modern human ilium so far examined. Correspondingly, the horizontal iliac bar which runs posteriorly from the acetabulum above the greater sciatic notch to the posterior iliac spine is very stout and well buttressed. Within the right angle enclosed by the vertical iliac pillar and the horizontal iliac bar the iliac fossa is very thin; the blade of the ilium has the characteristic hominid S-shape and it is set at a wide angle to the plane of the acetabulum.

The anterior superior iliac spine is missing but it may have been raked forward as suggested by the line of the anterior border as it runs upward from the anterior inferior iliac spine. The anterior inferior iliac spine is distinct and rounded showing a clear marking for the upper attachment of the iliofemoral ligament of the hip joint and another for the straight head of rectus femoris. To the lateral side of the spine the attachment of the reflected head of this muscle can be clearly traced above the acetabulum. Otherwise the gluteal aspect of the bone discloses a posterior gluteal line separating the attachments of gluteus maximus and gluteus medius as well as a middle

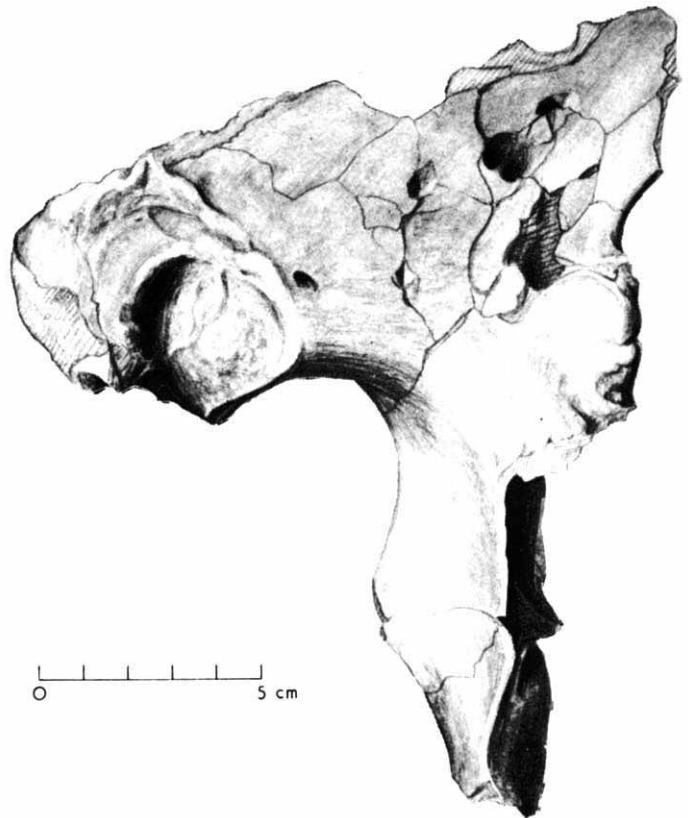


Fig. 4 Hip bone of Olduvai Hominid 28, pelvic surface. (Drawn by Audrey Besterman.)

gluteal line separating the attachments of gluteus medius and minimus. The pelvic aspect of the ilium shows a wide and shallow groove anteriorly for the iliopsoas muscle medial to the anterior inferior iliac spine; just below and behind the groove the iliopectineal line can be detected. In modern man this line is usually extended posteriorly as a ridge that separates the iliac fossa from the true pelvic wall, but in Olduvai Hominid 28 this ridge is missing; the iliac fossa runs smoothly down towards the greater sciatic notch and there is no excavation of the fossa above the horizontal iliac bar.

Posteriorly the auricular surface is small, set low on the bone and is slightly obliquely placed. It is also extended laterally round the inferior border of the ilium. This extension of the auricular surface is at an angle of approximately 120° to the principal part of the surface and would seem to limit relative movements of the sacrum and ilium in a vertical direction. Behind the auricular surface the ilial tuberosity is large and very roughened for the attachment of extensive posterior sacroiliac ligaments. There is no pre-auricular sulcus.

Sexing the hip fragment proved difficult, partly because the pubis is missing. There are a series of contradictory features such as a general robusticity (male), wide sciatic notch (female), large acetabulum (male), auricular surface small and obtuse (female), but, on balance, it seems more likely that it is female though the matter is still open.

An X-ray of the pelvic fragment disclosed several interesting features, some of which confirm the anatomical findings; for example, the stout horizontal iliac bar and the ischium are reinforced by coarsely woven internal trabeculae, and the vertical iliac bar is heavily buttressed with dense bone.

Functional Considerations

The combination of features that characterize the hip bone and the femur allows some functional conclusions to be drawn. These conclusions are strengthened if the two bones are

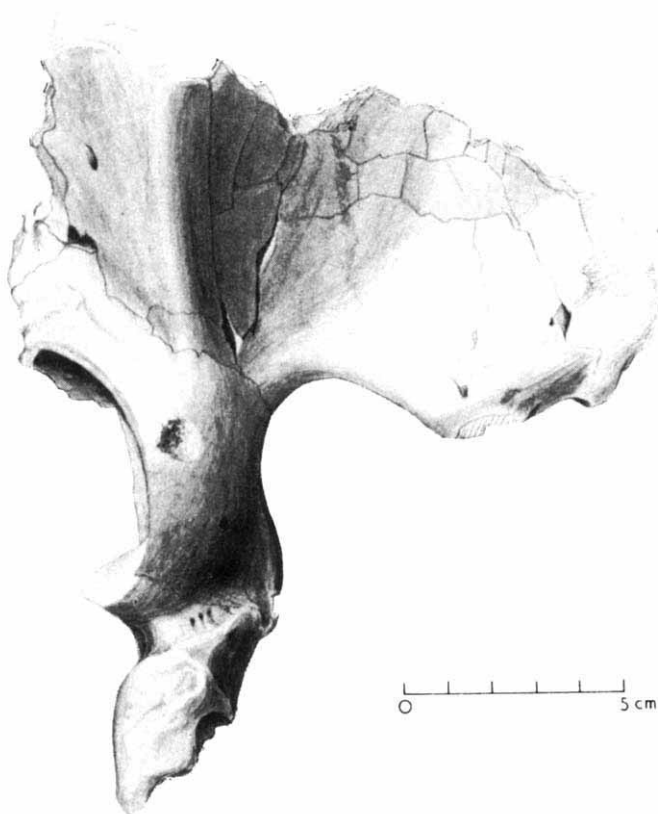


Fig. 3 Hip bone of Olduvai Hominid 28, gluteal surface. (Drawn by Audrey Besterman.)

assumed to belong to the same individual; anatomically they are not incompatible and both belong to the left side, and because they were found in close association in the deposit it would seem reasonable and economical to assume that they belong with each other. It is suggested therefore that:

(1) The strength of the vertical iliac pillar, to resist the pull of gluteus medius, gluteus minimus and tensor fascia lata, coupled with the femoral expansion for the lower attachments for gluteus medius and minimus muscles, suggests that the alternating pelvic tilt mechanism of striding bipeds was well developed.

(2) The length and strength of the horizontal iliac bar, coupled with well marked attachments for gluteus maximus (on both hip bone and femur) and the hamstring muscles, indicate a powerful hip extensor mechanism for returning the trunk to the erect position and/or raising the trunk (as in walking uphill or climbing).

(3) The impressions for the iliofemoral ligament on both hip and femur suggest that the pelvic rest mechanism of advanced bipeds was fully developed and that the centre of gravity of the body was placed behind the line joining the rotation centres of the two hip joints.

(4) The rugged area for the attachments of the sacroiliac ligaments shows that the weight of the upper part of the body was being transferred to the pelvis by way of the sacral suspensory mechanism familiar in upright bipeds.

(5) The attachments of ilio-psoas and rectus femoris muscles indicate the power of hip flexion, and the rectus femoris muscle coupled with vastus medialis and lateralis muscles indicate that powerful extension of the knee was possible.

In summary there seems little doubt that Olduvai Hominid 28 was a habitual upright biped. Whether bipedalism in this form was as efficient as that of modern man will not be determined until these bones have been reconstructed and some of their special features fully explained in biomechanical terms, that is, the extremely strengthened vertical pillar, the medial rotation of the ischium and the like.

Comparative Anatomy

Comparisons have been made with a series of modern human femora and with the following.

(1) Originals: Trinil femora (I–VI); Rhodesian femora; Tabun I femur; Olduvai Hominid 20 femur; and the Skhul IX femur.

(2) Casts and descriptions: Choukoutien femora; Krapina femora (1049 and II); Swartkrans femora; Spy II femur; Skhul IV femur; and the Kanjera femur.

Comparisons have also been made with a series of modern human hip bones and with the following pelvic remains.

(1) Originals: Rhodesian; Tabun.

(2) Casts: Swartkrans; Sterkfontein; Makapansgat; and Kromdraai.

Although some of the individual anatomical features of both the femur and pelvic fragment of Olduvai Hominid 28 can be matched in the comparative material, there is no doubt that it is only with the femora of the Choukoutien group of *Homo erectus* that the combination of features of the femur of Olduvai Hominid 28 can be closely paralleled. The combination of features of the Olduvai Hominid 28 pelvis is, however, so far unmatched in the comparative material studied.

It is established beyond reasonable doubt that the Choukoutien femora are part of the same assemblage as the Choukoutien *Homo erectus* cranial and dental remains³ and can be assigned to the Middle Pleistocene⁵. In the meticulous descriptions of the Choukoutien postcranial remains, Weidenreich makes plain (1) that the femora must be attributed to a member of the genus *Homo*, and (2) that they are specifically distinct from the femora of *Homo sapiens*. On these grounds the bones were attributed, with the cranial and dental remains, to "*Sinanthropus pekinensis*". In his summary Weidenreich lists a number of features that he states are specific for this taxon.

It is of interest to compare these features with the corresponding features of Olduvai Hominid 28 (Table 1).

Of these points, five agree completely, three are in partial agreement (mostly because of lack of evidence) and the sole point in disagreement is subject to considerable anatomical variability.

Table 1 Comparison between *Homo erectus pekinensis* and Olduvai Hominid 28

<i>Homo erectus pekinensis</i>	Olduvai Hominid 28
(1) Straightness of the shaft (that is, lack of marked A/P bowing)	Agrees
(2) The distal position of the least breadth of the shaft	Agrees
(3) Convexity of the medial border of the shaft	Agrees
(4) Pronounced platymeria of the subtrochanteric region combined with angularity (medial and lateral cristae)	Agrees
(5) (i) Development of a hypotrochanteric tubercle at the base of the greater trochanter	(i) Uncertain
(ii) The direct continuation of the hypotrochanteric crest into the greater trochanter	(ii) Agrees
(6) Absence of linea intertrochanterica and linea pectinea	Disagrees
(7) Extraordinary thickness of the wall of shaft and the neck combined with the narrow calibre of the medullary canal	Unusual neck thickness present, walls of moderate thickness, canal of moderate calibre
(8) Diffuse arrangement of the trabecular system of the upper end combined with a tight-meshed and coarse cancellous substance	Specimen incomplete, but radiographic evidence is not inconsistent

Thus the group of features said by Weidenreich to be specific for Choukoutien *Homo erectus* are shared in large part by Olduvai Hominid 28 and are not found together in *Homo sapiens*. Furthermore, all the metrical features quoted by Weidenreich for Choukoutien *Homo erectus* fall within the range of variability quoted by him for *Homo sapiens*; but the important point made by him (before the advent of multivariate statistics in the assessment of affinity) was that it is the combination of features in Choukoutien *Homo erectus* that differs from the combination of features in *Homo sapiens*.

The femora that must be considered closely are the six femora from Trinil, Java^{2,6–11}. It is primarily on these bones that there rests the widely held view that the lower limb of *Homo erectus* differed little from that of modern man, a view that depends in turn on the contemporaneity of the femora with the Trinil calotte, their proper attribution to a Middle Pleistocene date, and a morphological appraisal that considers these femora to be essentially sapient.

Through the kindness and courtesy of the director of the Leyden Museum I have been able to re-examine the Trinil femora both anatomically and radiologically. The preliminary results of this examination reaffirm that these femora have no significant anatomical, radiological or metrical features that lie outside the known range of variation for modern man, nor do they show any combination of features that constitutes a taxonomically or functionally significant morphological pattern. Further work is in progress, in conjunction with Miss Theya Molleson, of the British Museum (Natural History), in order to try to clarify the position by reviewing the evidence for the supposed provenance of the Trinil femora, and by reassessing their relative and absolute dating.

The Olduvai Hominid 28 femur clearly bears remarkable similarities to the well established *Homo erectus* femora from Choukoutien, anatomically, metrically (Table 2) and radiologically. At the same time the Olduvai Hominid 28 pelvic fragment shows a number of anatomical and radiological features that distinguish it from modern sapient pelvises, but

Table 2 Comparison of Femora

Martin Nos. (1928)	Length (mm)	Subtrochanteric region			Mid shaft region			Torsion	Curva- ture	Femoral indices			
		Trans.	Sagitt.	Circum.	Trans.	Sagitt.	Circum.			Length/ thickness index (8) × 100	Robusticity index (6+7) (2) × 100	Platymetric index (10) (9) × 100	Pilastric index (6) (7) × 100
Olduvai Hom. 28	456*	37.4	23.3	99.0	32.7	24.7	95.0	> 18°	2.91	20.8	14.8	62.3	75.5
Trinil I	455	—	—	—	28.0	29.0	89.0	25°	1.77	19.6	12.5	—	103.6
Trinil II	460*	32.7	26.2	95.0	27.1	26.2	85.0	—	1.75	18.5	11.6	80.1	97.0
Trinil III	—	32.2	24.2	92.0	27.7	25.4	85.0	—	1.53	—	—	75.2	91.7
Trinil IV	—	33.7	23.8	92.0	28.4	25.7	87.0	—	1.50	—	—	70.6	90.5
Trinil V	—	—	—	—	26.3	27.0	85.0	—	—	—	—	—	102.6
Peking I	c. 400	34.3	23.2	90.0	29.7	27.1	98.0	—	—	24.5?	14.2?	67.6	91.2
Peking II	—	—	—	—	26.4	22.8	77.0	—	—	—	—	—	86.4
Peking IV	407*	34.3	22.7	94.0	29.3	25.0	85.0	35°/36°	2.25	20.9	13.4	66.2	85.3
Peking V	—	—	—	—	29.5	23.7	83.0?	—	—	—	—	—	80.3
Peking VI	—	—	—	—	29.2	26.1	85.0	—	—	—	—	—	89.4

* Reconstructed.

there are no known examples of *Homo erectus* pelvic remains from elsewhere with which to make comparisons.

It seems reasonable therefore to suggest that the morphological affinities of Olduvai Hominid 28 lie with *Homo erectus* from Choukoutien and that it should be attributed to this specific taxon. Only a full re-examination of the morphology and dating of the Trinil femora may enable the taxonomic position of this material to be established because they appear, perhaps as they always did, to have little in common with the *Homo erectus* femora from Choukoutien.

I thank Mrs Mary Leakey for allowing me to examine this material and Dr W. G. S. Hopkirk (Nairobi Hospital) and Dr Alan Walker (Department of Anatomy, University of Nairobi) for their help.

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- ¹ Leakey, M. D., *Nature*, **232**, 380 (1971).
- ² Dubois, E., *Pithecanthropus erectus-eine Menschaehnliche Ubergangsform aus Java* (Landesdruckerei, Batavia, 1894).
- ³ Weidenreich, F., *Palaeont. Sin.*, New Ser. D, **10**, 1 (1941).
- ⁴ Brothwell, D. R., Molleson, T., and Metrewelli, C., in *The Skeletal Biology of Earlier Human Populations* (edit. by Brothwell, D. R.), 173 (Pergamon, Oxford, 1968).
- ⁵ Kurtén, B., and Vasari, Y., *Commentat. Biol.*, **23**, 1 (1960).
- ⁶ Dubois, E., *Proc. Acad. Sci. Amst.*, **29**, 730 (1926).
- ⁷ Dubois, E., *Proc. K. Ned. Akad. Wet.*, **29**, 1275 (1927).
- ⁸ Dubois, E., *Proc. K. Ned. Akad. Wet.*, **35**, 716 (1932).
- ⁹ Dubois, E., *Proc. K. Ned. Akad. Wet.*, **37**, 139 (1934).
- ¹⁰ Dubois, E., *Proc. K. Ned. Akad. Wet.*, **38**, 850 (1935).
- ¹¹ Dubois, E., *Proc. K. Ned. Akad. Wet.*, **40**, 864 (1937).

Spatial Discrimination in the Cytoplasm during Microtubule Morphogenesis

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Patterns of microtubule formation and breakdown in the ciliate *Nassula* provide some indications of the ways in which the deployment of substances influencing microtubule assembly is related to control of tubule growth.

DETAILS of microtubule distribution during the fission cycle in the ciliate *Nassula*¹⁻⁶ provide striking examples of how the precise spatial and temporal controls of assembly and breakdown of several microtubular organelles can be exercised simultaneously within a single cell. These findings raise fundamental issues concerning control of the ways in which microtubule precursor protein subunits, and other substances affecting microtubule stability, encounter the sites where tubules are growing or dissociating.

It is generally supposed that structural molecules are synthesized on ribosomes distributed throughout the cytoplasm

and that these, and all other molecules influencing the growth and stability of organelles, reach their sites of action by random diffusion through the cytoplasm. This supposition has never been seriously challenged. It seems especially reasonable because several structural molecules, microtubule subunits included⁷, self-assemble *in vitro* to form structures identical in many respects with those developing *in vivo* when this assembly is seeded by portions of the structures in question. In addition, there are indications that, in some cells, the distribution and form of certain nucleating sites define the positioning of the microtubules which grow out from them *in vivo* by providing sites which seed tubule assembly^{3,4,8}. The positioning of these nucleating sites is probably crucial to the control of the number and location of microtubules. This article is not concerned with how nucleating sites act, or how they are distributed, but with the localization of microtubule subunits, and any other molecules influencing their assembly, at the sites where assembly or dissociation of these subunits is occurring. Some of the morphogenetic events described here, which are probably paralleled in other cells, cannot be entirely accounted for by the interaction of randomly diffusing molecules with a set of nucleating sites and mature and growing microtubular organelles.

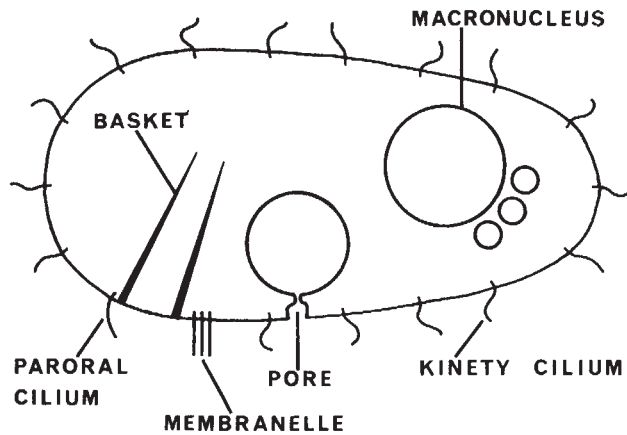


Fig. 1 Diagrammatic median longitudinal section of an interfission *Nassula*. Its anterior end is to the left and its ventral surface towards the bottom of the figure.

Nassula during the Cell Cycle

Nassula possesses a single macronucleus (Fig. 2, *m*) with three adjacent micronuclei. Most of the other large organelles are attached to the pellicle (Fig. 1). The contractile vacuole pore (Fig. 5, *c*) is a pellicular invagination connecting to the vacuole. A feeding organelle, the cytopharyngeal basket, consists largely of a circular palisade of rod-shaped microtubule bundles (Figs. 2, 3 and 4). A row of paroral cilia (*p*) flanks the oral opening (*o*) and a row of ciliary membranelles (*x*) passes just over halfway around the organism (Fig. 5). Rows of cilia called kineties extend from one end of the organism to the other; basal bodies in the same kinety are linked by bands of microtubules.

Many of the changes in microtubule organization during binary fission, summarized here with the aid of Fig. 6, occur simultaneously. At 20° C all take place within 2 h of the start of fission, except the growth of new baskets, which continues for another 2.5 h. The old basket (1) detaches from the pellicle and two new baskets (2) develop. In each region where a new basket develops, a set of new rods initially forms a series of short rows, which align to form a single long row, which then rolls up to form a circular palisade.

Spindle tubules form and break down inside the macronucleus (3) and three micronuclei (4) while nuclear membranes remain intact. Morphogenesis of all the other microtubular organelles considered here occurs in a common continuously streaming cytoplasm. No membranes partition this cytoplasm to prevent molecules diffusing between these organelles. While nuclei divide, three types of tubule arrays develop just before, and break down shortly after, they are spatially associated with changes in cell shape or movement of cytoplasmic structures. A reticulum of microtubules (5) interconnects growing cytopharyngeal rods as they roll up to form two new baskets (2). Simultaneously microtubular strands (6) contact contractile vacuole pores as pores move posteriorly for about 30 µm, while a microtubular girdle (7) forms at the base of the cleavage furrow. Also, new microtubules are augmenting the bands (8) to link permanently new and old kinety basal bodies.

If tubule subunits in each type of array differ from those in other arrays, assembly of appropriate amounts of each species of subunit at the sites, where only they can assemble, may be largely determined by the amounts synthesized. Even if subunits are synthesized more or less randomly throughout the cytoplasm, approximately equal quantities of a subunit species will by random diffusion encounter each appropriate assembly region. But if the tubules in these several arrays are of identical composition, control of the distribution of subunits to assembly sites must be more refined; at least as refined as that which controls the morphogenesis of cilia, basal bodies and cyto-

pharyngeal microtubules. There are important instances involving these structures where initially identical tubules develop in one cytoplasmic region and simultaneously break down in another. For example, old cytopharyngeal baskets (1) gradually break down for 1 h while new ones (2) develop. Even some new cytopharyngeal rods (9) break down while the remainder continue lengthening; these are errant rods which have not been included in a new circular palisade during rolling up. Neither old baskets nor errant rods are enclosed in vacuoles while they break down. Paroral cilia and their basal bodies (10) develop about 1 h before any of the others, while only the cilia of the old membranelles (11) break down and the old kinety cilia (12) remain intact. Subsequently new membranelles (13) and kinety cilia (14), and new cilia forming on old membranelle basal bodies (11), all develop at about the same time. It is difficult to account for these events if it is assumed that tubule

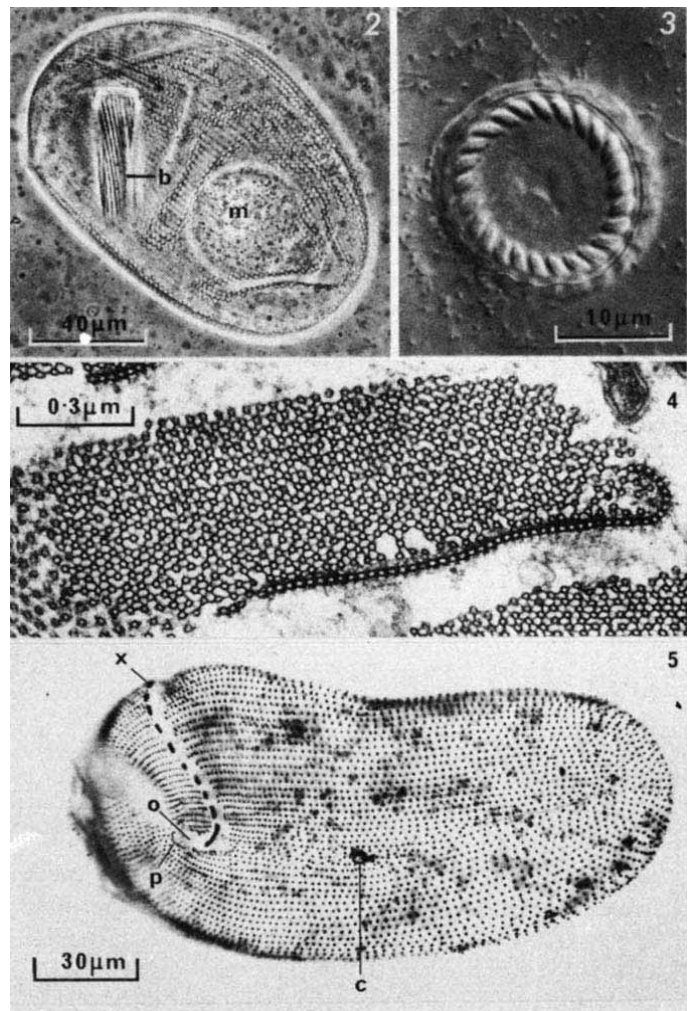


Fig. 2 An interfission *Nassula* after cold ethanol digitonin treatment⁹ which dissolves most cytoplasmic components and leaves a pellicular ghost enclosing the cytopharyngeal basket (*b*) and the macronucleus (*m*). The top of the basket, which is attached to the pellicle, is towards the top of the figure. Phase contrast.

Fig. 3 The circular palisade of rods in a living *Nassula* at the top of a cytopharyngeal basket, viewed from above. Numerous cilia are also shown. Nomarski interference contrast.

Fig. 4 A microtubular cytopharyngeal rod in cross-section. Electron micrograph.

Fig. 5 The ventral surface of an interfission *Nassula* with its anterior end to the left and its left side towards the top of the figure. The pellicle is stained with silver¹⁰ around the rim of the contractile vacuole pore (*c*) and where it is penetrated by cilia. A row of paroral cilia (*p*) flanks the oral opening (*o*). A row of ciliary membranelles (*x*) and numerous rows of kinety cilia are also shown. Bright field.

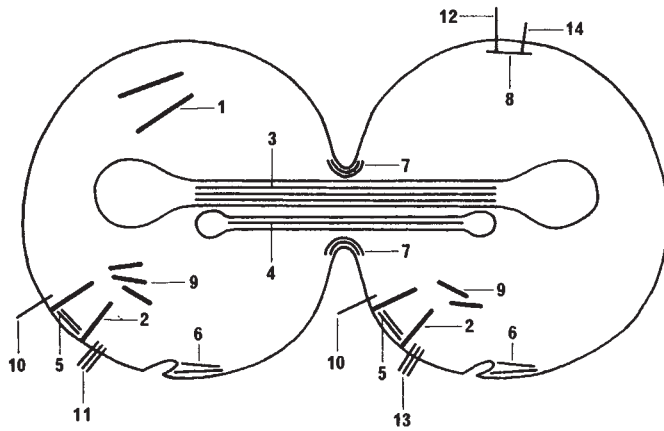


Fig. 6 Schematic diagram of a median longitudinal section of a dividing *Nassula* showing the positions of the majority of its microtubular organelles. The organism is oriented as in Fig. 1. For clarity contractile vacuoles have been omitted, and only two kinety cilia and one of the three micronuclei have been included. The lines indicating the positions of microtubular arrays and organelles also show the orientation of the longitudinal axes of the tubules but provide no indication of the numbers of tubules involved. Old cytopharyngeal basket, (1); new cytopharyngeal basket, (2); macronuclear spindle, (3); micronuclear spindle, (4); microtubular reticulum associated with rolling up of new cytopharyngeal rods, (5); microtubular strand associated with posteriorly directed movement of contractile vacuole pore, (6); microtubular girdle at the base of the cleavage furrow, (7); microtubular band linking kinety basal bodies, (8); errant rods, (9); paroral cilium, (10); old ciliary membranelle, (11); old kinety cilium, (12); new membranelle, (13); new kinety cilium, (14).

subunits are synthesized more or less randomly throughout the cytoplasm, and that they, and all agents which affect tubule stability, reach tubules and tubule nucleation sites by simple diffusion through the cytoplasm. There must be special ways of concentrating these materials in discrete cytoplasmic regions without partitioning these regions off from the remainder of the cytoplasm by membranes. Analyses of cytopharyngeal morphogenesis, now being undertaken, suggest ways in which such concentrations may be achieved.

Cytopharyngeal Microtubules

When dividing organisms are immersed in aqueous solutions of colchicine (5 mg/ml.), assembly of cytopharyngeal tubule subunits is completely inhibited. Tubules subsequently attain normal lengths after assembly has been delayed for 1 h if organisms are returned to their normal culture medium (water). Immersion in aqueous solutions of cycloheximide (5 µg/ml.) greatly reduces the rate of subunit assembly, and when assembly ceases the tubules are much shorter than is normally the case. In some experiments assembly was delayed by using colchicine for 1 h just after assembly had started, and then colchicine was leached out of the organisms while simultaneously cycloheximide was applied. Tubules finally attained the same lengths as they did in organisms in which subunit assembly had proceeded normally for the first hour of development before cycloheximide was administered. Thus there is an increase in the amount of tubule subunit assembly occurring in the presence of cycloheximide following a 1 h delay of assembly induced by colchicine. Hence cycloheximide probably does not interfere directly with assembly in a marked fashion, and is almost certainly inhibiting assembly by blocking synthesis of proteins, possibly tubule subunits, which is occurring while subunits assemble. Cycloheximide acts in this manner during flagellar regeneration in *Chlamydomonas*¹¹. While assembly is most sensitive to cycloheximide in *Nassula*, ribosome-bearing cisternae of endoplasmic reticulum are clustered around the tips of tubules where subunit assembly occurs. Thus tubule subunits, or materials which stabilize their assembly, may be

synthesized on particular ribosomes and not released until the ribosomes are very close to the tubule assembly points.

Errant rods move away from new baskets before breaking down. If organisms are immersed in aqueous solutions of vinblastine sulphate (10 µg/ml.) this movement does not occur and errant rods remain intact. The agents provoking breakdown have probably not been inactivated, for the more lengthy breakdown of the much larger old baskets still proceeds under these conditions. Thus it seems that these agents are strictly localized in particular cytoplasmic regions. To account for the spatial discrimination involved in selective breakdown of this kind there is little alternative but to postulate the operation of sophisticated procedures. For example, breakdown of errant and old rods, but retention of new baskets, could be accomplished if the agents promoting breakdown have a relatively short active life, and are only present and bound to the nuclear envelopes for about 90 min from the start of fission. Errant and old rods may contact the envelopes of the centrally positioned nuclei but new short baskets attached to the pellicle cannot do so (Fig. 6). It is also necessary to postulate that the agents are only released from nuclear envelopes when contacted by tubules, to which they attach, and then progressing along tubules cast off subunits behind them, while remaining attached to the contiguous tubule remnants until their deactivation is induced by fragmentation of the final portions of tubules. It is significant that *in vivo* cytopharyngeal tubules break down progressively from their tips³.

Experiments to test these hypotheses are in progress. In the meantime it is worth bearing in mind the possibility that the distribution of molecules involved in organelle morphogenesis may often be extensively governed by their being bound to larger structures up to the point at which they interact with a mature or growing organelle.

Other Cells

To what extent are the events described here typical of cells generally? The large size of some of the organelles involved is certainly unusual, but the information required to specify that a bundle of about 10 microtubules about 10 µm long grows out from a particular site at a particular phase of the cell cycle need not be greatly augmented to ensure that the development of a bundle of about 1,000 tubules about 100 µm long is equally precisely controlled. It is also worth noting that very precisely controlled patterns of simultaneous microtubule formation and breakdown are known to occur in the cells of certain multicellular organisms, for example¹², and for spindles, at least, we know that control of tubule deployment is very exact.

Egg cytoplasm differentiates into regions of different composition sometimes characterized by distinct groupings of ribosomes and other organelles¹³. Patterns of egg cytoplasm differentiation are spatially related to patterns of cell differentiation in embryos. Mechanisms defining cytoplasmic patterns in eggs may be similar to those controlling microtubule arrangement in cells generally.

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- ¹ Tucker, J. B., *J. Cell Sci.*, **2**, 481 (1967).
- ² Tucker, J. B., *J. Cell Sci.*, **3**, 493 (1968).
- ³ Tucker, J. B., *J. Cell Sci.*, **6**, 385 (1970).
- ⁴ Tucker, J. B., *J. Cell Sci.*, **7**, 793 (1970).
- ⁵ Tucker, J. B., *J. Cell Sci.*, **8**, 557 (1971).
- ⁶ Tucker, J. B., *J. Cell Sci.* (in the press).
- ⁷ Stephens, R. E., *Quant. Rev. Biophys.*, **1**, 377 (1969).
- ⁸ Tilney, L. G., and Goddard, J., *J. Cell Biol.*, **46**, 564 (1970).
- ⁹ Child, F. M., and Mazia, D., *Experientia*, **12**, 161 (1956).
- ¹⁰ Chatton, E., and Lwoff, A., *CR Séanc. Soc. Biol.*, **118**, 1068 (1935).
- ¹¹ Rosenbaum, J. L., Moulder, J. E., and Ringo, D. L., *J. Cell Biol.*, **41**, 600 (1969).
- ¹² Ledbetter, M. C., in *Formation and Fate of Cell Organelles* (edit. by Warren, K. B.), 55 (Academic Press, London, 1967).
- ¹³ Mahowald, A. P., and Hennen, S., *Devel. Biol.*, **24**, 37 (1971).

LETTERS TO NATURE

PHYSICAL SCIENCES

Atmospheric Total Ozone Increase during the 1960s

NAMIAS¹ has postulated that sea-air interactions on a regional basis, and not necessarily air pollution, volcanic activity, or solar intensity variations, may have caused the cooling trend that was observed in numerous areas of the world during the past decade^{2,3}. In particular, he attributed the United States temperature anomaly, that is, lower than normal winter temperatures in the eastern two-thirds of the country, and higher than normal winter temperatures in the west, to intensification of the Rossby wave at the 700 mbar level. This intensification strengthens the ridge over western North America and deepens the trough to the east, thus increasing the frequency of deployment of Arctic air masses into the eastern United States. Namias attributed the change in the character of the Rossby wave to abnormal cyclonic activity that occurred in the winter atmospheric circulation over the North Pacific, the surface waters of which were unusually warm during the 1960s.

Because the effects of a deepened 700 mbar trough over the eastern United States might reasonably be expected to extend to higher altitudes, we considered the possibility that the increased southward flow of air in the troposphere and low stratosphere led to an average increase in total ozone amount over central and eastern North America during the 1960s. Ozone is transported poleward from the equatorial stratosphere source region in the winter hemisphere, before it descends to lower levels⁴. To determine whether an increase in total ozone occurred, we analysed data obtained during the decade 1961 to 1970 at Edmonton, Goose Bay, and Toronto, in Canada, and at Boulder, Bismarck, Green Bay, Caribou, Bedford, Nashville, and Tallahassee, in the United States. The periods of record ranged from 7 to 10 years for all stations except Tallahassee, where observations were made for only 5 yr. At eight of the ten stations, we found statistically significant increases in ozone that varied between 4.4% per decade at Goose Bay, to 8.8% per decade at Nashville, with an average increase for the eight stations of 5.6% per decade. At Green Bay and Toronto, although the calculated trends in ozone were not found to be statistically significant, they produced small positive values, 2.0% and 3.5% per decade, respectively.

To ascertain whether the trough deepening described by Namias extended into the low stratosphere, the geopotential heights of the 200, 100, and 50 mbar pressure surfaces at two stations—Caribou and Nashville—were investigated for the period January 1961 to August 1970. The results of the analysis suggest to us that trough intensification occurred at both stations, particularly during February and March and to a lesser extent in September, October, and November. During other months of the 10 year period, progressive weakening of the trough occurred.

Our total ozone data analyses also yielded statistically significant ozone increases during the 1960s at Dobson spectrophotometer stations distant from the North American continent. At Mauna Loa Observatory in Hawaii, the upward trend was 2.5% per decade, while at Huancaayo, Peru, the trend was 6.0%. Subsequent analyses of data from several foreign stations

(Fig. 1) confirmed that increases in ozone were not confined to the North American region, but were also characteristic of other areas of the world.

Fig. 1 shows mean monthly total ozone deviations from monthly normals, based on the periods of record indicated, for seven stations in the northern and southern hemispheres. The ozone monthly means were calculated, in most instances, from observations during 25 or more days per month; in isolated cases, however, the means were determined from as few as 10 days of observations. The ozone trend lines were fitted to the data by the least squares method. Table 1 summarizes the results.

Note that the calculated rates of ozone increase range from $2.4 \pm 0.6\%$ per decade at Mauna Loa Observatory in Hawaii, to $10.0 \pm 0.4\%$ per decade at Kodaikanal in India. Errors given with the trend figures are computed probable errors. In calculating the trends we have assumed that the calibration levels of the spectrophotometers, operated at the stations listed in Table 1, remained constant in time. Using the criterion that the sign of the ozone trend is significant, provided that it does not change within the range of ± 3 probable errors, the

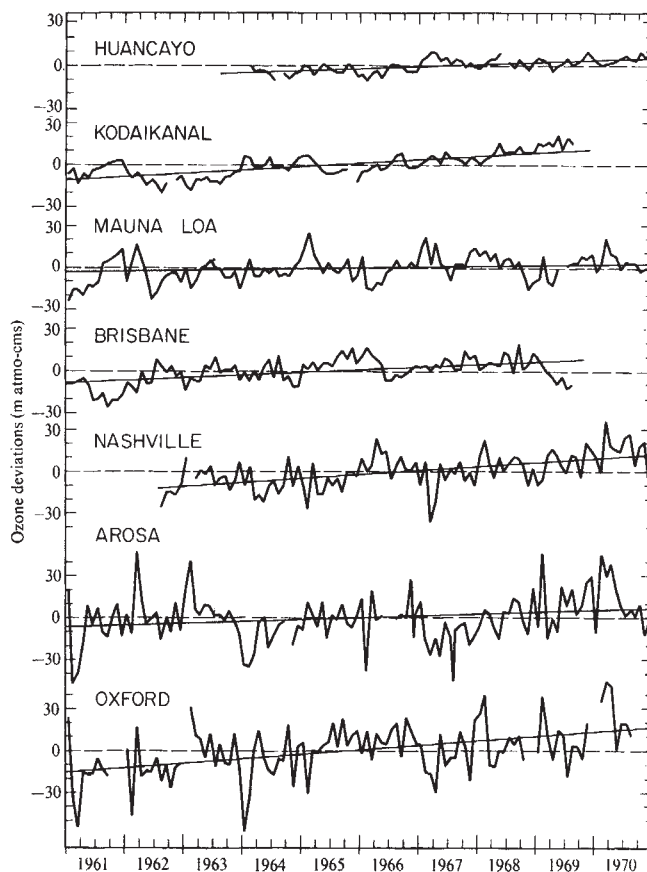


Fig. 1 Plots of mean monthly total ozone deviations from monthly normals for selected stations. Linear trend lines have been fitted to the data.

data clearly indicate that statistically significant increases in total ozone amount were detected at the stations listed in Table 1.

Table 1 Summary of the Data Analyses presented in Fig. 1

Station	Lat., long.	Mean O ₃ in m atmo- cms†	% O ₃ increase per decade*
Huancayo, Peru	12° 03' S, 75° 19' W	262	6.0±0.4
Kodaikanal, India	10° 14' N, 77° 28' E	257	10.0±0.4
Mauna Loa, Hawaii	19° 32' N, 155° 35' W	276	2.4±0.6
Brisbane, Australia	27° 28' S, 153° 02' E	289	6.6±0.6
Nashville, USA	36° 15' N, 86° 34' W	332	8.8±0.7
Arosa, Switzerland	46° 46' N, 09° 40' E	333	4.1±1.0
Oxford, England	51° 45' N, 01° 11' W	354	8.9±1.0

* Extrapolated from the periods of record shown in Fig. 1.

† The unit "m atmo-cms" or "milli-atmo-cms" is used to denote the total amount of ozone in a vertical column of the atmosphere, expressed as the thickness of the ozone layer at STP, assuming that the ozone is separated from the rest of the air.

Although additional data analyses yielded increases in ozone at most stations investigated, the results were not always statistically significant. For example, a small but statistically insignificant increase in ozone of $1.1 \pm 0.9\%$ per decade was calculated for Aspendale, Australia (38° 02' S, 145° 06' E). We also analysed data obtained at Tateno in Japan (36° 03' N, 140° 08' E), and Vladivostok in Siberia (45° 07' N, 131° 54' E). Both these stations lie near a region that, according to Namias, experienced a deepening of the 700 mbar trough during the past decade similar to the trough intensification that occurred over eastern North America. Although a positive trend in total ozone of $6.2 \pm 3.3\%$ per decade was computed for Vladivostok, we cannot classify this as significant under the criterion that it did not change sign within the range of ± 3 probable errors. For Tateno, on the other hand, a downward trend in ozone was calculated, also statistically insignificant, and of magnitude $-3.4 \pm 1.3\%$ per decade.

The tentative linear analyses of the North American total ozone data, as well as the analyses of the data from foreign stations shown in Fig. 1, suggest that an increase in total ozone occurred in many areas of the world during the past decade. This increase cannot be interpreted as an apparent ozone increase that has arisen because of errors in measurement associated with changing atmospheric turbidity. The fundamental method of measuring ozone with Dobson ozone spectrophotometers⁵, using wavelength pairs $A(3055 \text{ Å}, 3254 \text{ Å})$ and $D(3176 \text{ Å}, 3398 \text{ Å})$, is highly insensitive to scattering of solar radiation by particulate matter because, through the subtraction of two nearly equal terms, the scattering term that appears in the equation from which total ozone amounts are calculated is rendered negligibly small. The possibility that the computed rates of ozone increase are due to long term drift in spectrophotometer calibrations should, however, not be discounted. We recently compared the calibration level of our Caribou spectrophotometer with that of a standard spectrophotometer maintained at Boulder, Colorado, and found a drift in the calibration of the Caribou instrument. The magnitude and direction of the drift are such as to account for about one-half of the 5.9% calculated rate of ozone increase per decade at Caribou. In June 1970, on the other hand, the Nashville spectrophotometer was brought to Boulder and compared with our standard instrument. The intercomparison tests showed that the calibration level of the Nashville spectrophotometer did not change by more than 2% during 8 years of opera-

tion. Thus, the deduced 8.8% per decade increase in ozone at Nashville cannot be attributed, in large measure, to drift in instrument calibration.

A more comprehensive analysis than that presented here is needed to determine whether a global increase in atmospheric total ozone occurred during the past decade, or whether ozone increases in certain areas of the world were compensated by decreases in other areas. Such an analysis should not only involve data from the worldwide network of total ozone observatories, but should also take into account the calibration histories of the instruments with which observations were made. We are currently recalibrating our Dobson ozone spectrophotometers in an effort to determine the influence of drift in instrument calibrations on the accuracy of the North American ozone measurements.

The Huancayo station is operated in cooperation with the Instituto Geofísico del Peru.

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¹ Namias, J., *Science*, **170**, 741 (1970).

² Mitchell, jun., J. M., in *Global Effects of Environmental Pollution* (edit. by Singer, S. F.) (Springer, New York, 1970).

³ Wahl, E. W., and Lawson, T. L., *Mon. Weather Rev.*, **98**, 259 (1970).

⁴ Dütsch, H. U., in *World Survey of Climatology*, **4** (edit. by Landsberg, H. E.) (Elsevier, Amsterdam, 1969).

⁵ Dobson, G. M. B., and Normand, C. W. B., in *Annals of the International Geophysical Year*, **16**, 161 (Pergamon, Oxford, 1962).

Do Neutron Stars have an Ocean Surface?

This article draws attention to one of the more important unsolved problems concerning the qualitative nature of the outer layers of a neutron star. We refer to the likelihood of there being a vapour-liquid type phase transition, involving a major density discontinuity by a factor that could be as high as three or more, between the crust (in which starquakes are thought to take place) and the neutron superfluid below. The idea that such a phase discontinuity might exist is not new¹, but the question does not seem to have been taken seriously in recent years. This is due to the absence of discontinuities not only in the highly simplified but historically important equations of state of Harrison and Wheeler² and of Tsuruta and Cameron³ which played such an important role in discussions of neutron star structure in the period extending up to the mid sixties, but also in the much more sophisticated equations of state which have been published in recent years, such as those of Langer, Rosen, Cohen and Cameron⁴, Bethe, Borner and Sato⁵, and Wang, Rose and Schlenker⁶.

We wish to make clear that the issue is still far from closed and that the existence of a major discontinuity is not only possible but even probable. The general problem of vapour-liquid type phase transitions in many fermion systems has recently been the subject of a reappraisal by Baker and Kahane⁷. They give naive but cogent reasons for expecting the existence of a discontinuous phase transition in any system of fermions where the interparticle forces are predominantly attractive at medium ranges but repulsive at short ranges: conditions which are believed to hold in a real neutron gas. This simple reasoning cannot, of course, be conclusive (the

chief element of doubt being in the question of how, when the forces have a complicated anisotropic form, one defines "predominantly"), but on the other hand, according to Baker and Kahane, the accuracy and convergence properties of the Brueckner-type expansion calculations, on which most of the present day continuity-free equations of state are based, are necessarily questionable in the neighbourhood of a real discontinuity. Furthermore, the most recent calculation along traditional lines, that of Baym, Bethe and Pethick⁸, predicts a first order phase transition (although their density is discontinuous by a very small fraction, quite unlike the order of magnitude change which we have in mind). What is clear is that considerably more elaborate techniques will be needed to decide conclusively whether or not neutron star matter has a large first order phase discontinuity between sub-nuclear and nuclear densities.

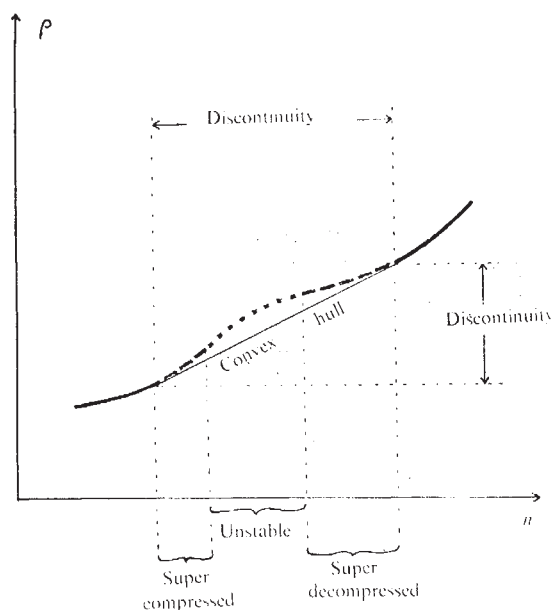


Fig. 1 Typical form of an equation of state with a first order phase transition.

It is worth emphasizing that we are not suggesting that the best present day equations of state are grossly unreliable in the sub-nuclear to nuclear density range (10^{11} to 10^{14} g cm⁻³) as they are at higher densities where hyperons and other high energy phenomena are important. The point is that quite a small alteration in the basic equation of state—which consists of an expression for the ground state energy density ρ as a function of baryon number density n —can introduce or remove a large density discontinuity. To make this clear we recall the standard principle (see, for example, ref. 2) that the necessary and sufficient condition for the absence of a discontinuity is that the curve of ρ against n be everywhere convex downwards. States where the curve is concave are locally unstable, and states where the curve is convex, but within and not on the convex hull, are only metastable (corresponding to super-compressed or superdecompressed states). Hence no states off the convex hull can exist in a stationary situation and nearly all methods of approach predict that the ρ - n curve is almost straight in the density range from 10^{11} to 10^{14} g cm⁻³ so the distinction between convexity and concavity is a fine one. For example, the ρ - n curve of Baym, Bethe and Pethick deviates from a straight line over the range 1.3×10^{14} to 3.9×10^{14} g cm⁻³ by an amount corresponding to at most about 1.2 MeV per baryon. This means that energy corrections of this order of magnitude, which corresponds to about 10%

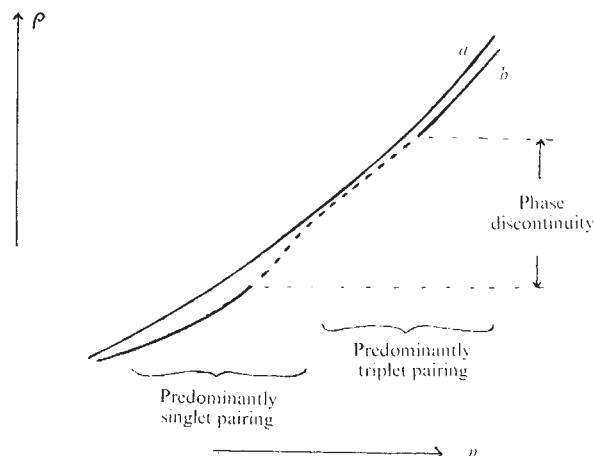


Fig. 2 Sketch illustrating (on an exaggerated scale) the qualitative form of the correction to the equation of state which can be expected to result from taking Cooper pairing energy into account. The convex curve *a* represents the uncorrected equation; the partly concave curve *b* represents the corrected equation.

of the total non-rest mass energy, would be sufficient to introduce a density discontinuity over a comparable range.

No one would claim that even the best present day equation of state calculations are reliable to within one MeV per baryon. Corrections of this order can come from many subtle effects such as three body interaction energies and Cooper pairing energies. Moreover, it would appear that the contribution from this latter effect is indeed of such a form as to introduce a concavity into the ρ - n curve, because the curve of pairing energy density against baryon number density can itself be expected to have a concavity due to the changeover from relatively strong singlet pairing at sub-nuclear densities to relatively weak triplet pairing at nuclear densities⁹. It may well be that this effect is not quite large enough, or that it is cancelled out by other fine corrections. Nevertheless it seems at least very likely that this effect really does introduce a significant phase discontinuity.

Such a discontinuity would be in many ways analogous to the terrestrial ocean surface, and as such might admit gravity waves, provided that the mechanism (such as a starquake) by which they were generated could release sufficient energy to dissolve the crystal structure at the base of the crust.

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- ¹ Salpeter, E. E., *Ann. Phys.*, **11**, 393 (1960).
- ² Harrison, B. K., Thorne, K. S., Wakano, M., and Wheeler, J. A., *Gravitation Theory and Gravitational Collapse* (University of Chicago Press, 1965).
- ³ Tsuruta, S., and Cameron, A. G. W., *Canad. J. Phys.*, **43**, 2056 (1965).
- ⁴ Langer, W. D., Rosen, L. C., Cohen, J. M., and Cameron, A. G. W., *Astrophys. Space Science*, **5**, 259 (1969).
- ⁵ Bethe, H. A., Borner, G., and Sato, K., *Astron. Astrophys.*, **7**, 279 (1970).
- ⁶ Wang, C. G., Rose, W. K., and Schlenker, S. L., *Astrophys. J. Lett.*, **160**, L17 (1970).
- ⁷ Baker, G. A., and Kahane, J., *J. Appl. Math.*, **10**, 1647 (1969).
- ⁸ Baym, G., Bethe, N. A., and Pethick, C. J., *Nuclear Phys.* (in the press).
- ⁹ Hoffberg, M., Glassgold, A., Richardson, R., and Ruderman, M., *Phys. Rev. Lett.*, **25**, 775 (1970).

The Hubble Constant and X-rays from Galaxy Clusters

X-RAY measurements and limits on the Coma and Virgo clusters of galaxies have been said to limit the mass of hot gas in them to 2% of the amount required for stabilization according to the virial theorem¹. Such a conclusion is strongly dependent on the value of the Hubble constant H_0 . The linear diameter of the cluster D and the cluster mass M , estimated by the virial theorem, each vary as H_0^{-1} . Therefore, the density ρ has the dependence $\rho \sim H_0^2$. The predicted X-ray flux F from this gas is $\sim \rho M/R^2$, where R is the distance to the cluster. R varies as H_0^{-1} . We therefore have the relation

$$F \sim H_0^3 \quad (1)$$

Meekins *et al.*¹ appear to have used the value $H_0 = 95 \text{ km s}^{-1} \text{ Mpc}^{-1}$ found by van den Bergh², because they took $R = 70 \text{ Mpc}$. If Abell's value³ $H_0 = 47$ is used, the predicted flux is reduced by a factor of 0.12. A reduction of H_0 to a value as low as 20 is not inconceivable. Although clumpiness increases F/M^2 , the presence of helium as a mass fraction f reduces F for fixed M in the ratio $(1 - \frac{1}{2}f)$.

Meekins *et al.* measured a flux of $0.03 \text{ photons cm}^{-2} \text{ s}^{-1}$ almost entirely in the range 3–17 Å, and from other wavelength channels were able to state that the gas temperature exceeds $8 \times 10^6 \text{ K}$. For a flat counter response I have determined from standard bremsstrahlung formulae⁴ that it would take $2.6 \times 10^{47} \text{ g}$ of hydrogen at this temperature, uniformly distributed in a sphere of diameter 4 Mpc at the adopted distance of 70 Mpc, to produce this flux. This is four times the mass limit given by Meekins *et al.*¹, and is in clear disagreement because they gave a diameter of 5 Mpc and the actual counter response rises as the bremsstrahlung spectrum falls. A recalculation by Dr Meekins (private communication) based on the original assumptions and actual counter efficiency has confirmed that the mass estimate is higher than originally stated and in fact is increased to $7 \times 10^{47} \text{ g}$. On this basis, a value

$$H_0 = 38 \text{ km s}^{-1} \text{ Mpc}^{-1} \quad (2)$$

would suffice to give agreement with the virial theorem for the Coma cluster. Those who are sure, as I am not, that clusters of galaxies are stabilized by ionized gas may interpret the X-ray measurement of Meekins *et al.* as a measurement of H_0 .

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¹ Meekins, J. F., Fritz, G., Chubb, T. A., Friedman, H., and Henry, R. C., *Nature*, **231**, 107 (1971).

² van den Bergh, S., *Bull. Amer. Astron. Soc.*, **2**, 223 (1970).

³ Abell, G. O., and Eastmond, S., *Bull. Amer. Astron. Soc.*, **2**, 179 (1970). See also de Vaucouleurs, G., *Ap. J.*, **159**, 435 (1970).

⁴ Allen, C. W., *Astrophysical Quantities*, second ed., 100 (The Athlone Press, London, 1962). (A factor Hz^{-1} must be supplied in the units for j_ν .)

Mercury in Water of the Tidal Thames

WE have developed a method for the determination of traces of mercury, and have applied it to the tidal reaches of the River Thames. This article reports our observations of the concentrations of mercury and its partition between dissolved forms and that adsorbed on suspended particulate matter.

There is a background concentration of about 0.02 µg/kg mercury in natural waters^{1–3}, and some recent results⁴ showed values of 0.009 – 0.021 µg/l. for essentially dissolved mercury in sea and river water. In regions of mercury mineralization⁵, however, up to 100 µg/kg has been reported. Similar amounts are found as a result of industrial pollution¹. For this study we chose sampling sites ranging from river water at Teddington to seawater at Southend with intermediate stations at Woolwich and Gravesend. The effluent from the Northern Outfall Sewage Works which provides a major input into the Thames⁶ was also examined. To achieve uniform sampling conditions all samples were collected by officers of the Port of London Authority on one day (May 24, 1971) 0.5 h after the afternoon high water at each station. Mercury was determined in whole and in filtered water and the mercury associated with the particulate matter found by difference.

The concentration of mercury in filtered water was low in the river water at Teddington and the seawater at Southend, and higher at Woolwich and Gravesend (Table 1). The level of dissolved mercury in the Northern Outfall effluent (0.515 µg/kg) suggests that some mercury may be held in solution as organic complexes. At all stations most of the mercury was associated with the particulate matter. In waters of high chloride concentration 96–98% of the total mercury was in this form, the proportion being lower in the river water (87%) and in the sewage effluent (82%). The concentration of mercury in the suspended particulate matter varied significantly with 1.8 mg/kg in the river water at Teddington, 9.6 mg/kg in the seawater and 4.3 and 4.9 mg/kg at Woolwich and Gravesend. The seawater may have been affected by effluent from the Southend outfall. Particulate matter in the Northern Outfall effluent contained 35 mg/kg mercury. The total concentration of mercury in the effluent (2.85 µg/kg) was about sixty times that in the river water at Teddington but is comparable with the slightly below 1 µg/l. ⁷ reported for the Hyperion outfall, Los Angeles. Thames estuary water is only slightly stratified⁶ indicating a high degree of mixing, and the outfall is sited and operated to achieve a rapid dilution of the effluent.

Surface water was collected in a plastic container and transferred immediately to acid washed screw cap polypropylene bottles. For total mercury determination about 200 g was used. For dissolved mercury about 1 kg of water was filtered by pressure through a Whatman GFC filter, the collecting bottle

Table 1 Concentration of Mercury in Thames River Water

Miles from London Bridge	Station	Cl^- (mg/l.)	Particulate matter (mg/kg)	Total	Mercury found (µg/kg)			Calculated levels of mercury on particulate matter	
					Dissolved	Difference		mg/kg	% of total
–18.5	Teddington	39	21.6	0.045	0.006	0.039	1.8		87
9	Woolwich	3,610	73.1	0.328	0.013	0.315	4.3		96
11.5	N. Outfall	142	66.0	2.85	0.515	2.34	35.5		82
27	Gravesend	10,030	89.9	0.446	0.009	0.437	4.9		98
43	Southend	16,480	8.2	0.082	0.003	0.079	9.6		96

washed free of particulate matter with distilled water, and the filtered sample replaced. (Only 200 ml. of the filtered Outfall water was used.) Both sizes of sample were weighed, made normal in sulphuric acid by adding 50% v/v H_2SO_4 , and 0.05 normal in permanganate by adding 5% w/v KMnO_4 in water, then shaken for 1 h. This treatment dissolved elemental mercury, mercury salts, and organo-mercury compounds as Hg^{2+} . Excess permanganate and any MnO_2 formed were reduced by adding 30% H_2O_2 solution. A silver wire coil⁸ freed of mercury by heating was added to each bottle and the bottles shaken overnight. Up to this stage the samples remained in their collecting bottles, thus minimizing contamination and losses of mercury. Each coil was removed from the solution, washed with water and acetone and dried in air. Optimum conditions for the recovery of mercury were determined using ^{203}Hg tracer. Mercury amalgamated with the silver was driven off by heating the coil to roughly 250° C in a silica tube. The mercury vapour was passed in a stream of nitrogen through a cell of 15 cm light path, in an atomic absorption spectrophotometer. The mercury atomic absorption peak was recorded on a strip-chart recorder and the amount of mercury present determined by comparison with the peak heights of calibration standards. Blanks of distilled deionized water and standards of Hg^{2+} added to distilled deionized water were run through the complete procedure with each set of samples. Interference by non-atomic absorption was found to be negligible during experiments using an intermediate distillation onto gold, but a deuterium arc background corrector was used in the determinations. For 1 kg samples the standard deviation of the blank was 0.0014 $\mu\text{g/kg}$ and the coefficient of variation at the 0.050 $\mu\text{g/kg}$ level was 1.8%. Particulate matter was determined from the increase in weight of the GFC filters used to filter the 1 kg samples after drying at 110° C. Chlorosity was determined by titration of a separate sample of water using silver nitrate.

Examination of additional samples taken at the Victoria Embankment (Cleopatra's Needle steps) at low water showed that the suspended particulate matter contained 5.0 mg/kg mercury and the deposited sediment 0.20 mg/kg mercury. Both samples were in contact with water containing 0.017 $\mu\text{g/kg}$ dissolved mercury, the difference reflecting the proportions of fine particles in the two materials. Only 4% of the sediment passed through a 63 μm sieve. The level of 0.20 p.p.m. mercury is similar to values we have found in sediment samples from the outer Thames estuary, and to reported values for shales¹.

This study indicates that 82–97% of the mercury in tidal waters of the Thames is held on suspended particulate matter and that significant amounts of mercury are introduced in sewage effluent. Among aquatic organisms, filter feeders such as molluscs and tunicates are especially exposed to mercury in the particulate form, but as dissolved mercury is readily adsorbed onto particulate matter, the effects of mercury on photosynthesis and productivity of phytoplankton may be more important. Both these aspects of mercury accumulation warrant further investigation.

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- ¹ *US Geol. Survey Professional Paper 713* (1970).
- ² Jonasson, I. R., *Geological Survey of Canada, Paper 70–57* (1970).
- ³ Keckes, S., and Miettinen, J. K., *FAO Tech. Conf. Marine Pollution*, Rome (1970).
- ⁴ Burton, J. D., and Leatherland, T. M., *Nature*, **231**, 440 (1971).
- ⁵ Dall'Aglia, M., in *Origin and Distribution of the Elements* (edit. by Ahrens, L. H.), 1065 (Pergamon, Oxford, 1963).

- ⁶ Water Pollution Research Technical Paper No. 11, *Effects of Polluting Discharges on the Thames Estuary* (HMSO, London, 1964).
- ⁷ Klein, D. H., and Goldberg, E. D., *Env. Sci. Technol.*, **4**, 765 (1970).
- ⁸ Hinkle, M. E., and Learned, R. E., *US Geol. Survey Professional Paper 650D*, 254 (1969).

The Oxfordshire Coalfield

THE discovery of eight coal seams of workable quality in the Geological Survey Apley Barn Borehole^{1,2}, sunk in 1960–61 near Witney, prompted the recent sinking of a second borehole (1970–71) near Steeple Aston, Oxfordshire. This borehole is situated between Bicester and Chipping Norton some 14 miles north-east of the Apley Barn Borehole (Fig. 1). The exact site is 825 yards (750 m) at 254° from St Peter's Church, Steeple Aston (National Grid Reference SU 4687 2586). The geophysical Bouguer anomaly gravity contour map shows that the borehole lies in the eastern part of a low density area where a thick sequence of light sedimentary rocks could be expected. It was thought possible that this anomaly could be due to a thickening of the Coal Measures sequence as a whole and that perhaps even Middle Coal Measures (with valuable coal seams) could be developed. In the event, however, this hope has not been realized, and although Upper Coal Measures were proved the borehole has shown that the low density anomaly feature must be due to a thickening of Devonian and/or older sediments.

The sequence proved in the Steeple Aston Borehole is as follows: Jurassic and Permo-Triassic rocks to 751 feet 3 inches (228.98 m), Upper Coal Measures to 2,003 feet 6 inches (610.67 m), intrusive igneous rocks to 2,545 feet 4 inches (775.82 m), Upper Devonian rocks to 3,172 feet 3 inches (966.90 m) then further intrusive rocks to a final depth of 3,199 feet 3 inches (975.13 m). Previously the Apley Barn Borehole had proved 820 feet 10 inches (250.19 m) of Jurassic and Permo-Triassic rocks, Upper Coal Measures (including eight seams totalling 27 feet of coal) to 3,968 feet 7 inches (1,209.62 m), Upper Devonian to 4,408 feet 4 inches (1,343.66 m) and Lower Devonian to a final depth of 4,941 feet 8 inches (1,506.22 m). In spite of the thinner sequence of Upper Coal Measures contained in the Steeple Aston Borehole, seven coal seams of workable quality more than 2 feet thick were encountered: (1) a 2 feet 2 inches seam base at 896 feet 6 inches, (2) a 2 feet 10 inches seam base at 925 feet 10 inches, (3) a 3 feet 5½ inches seam base at 957 feet 4½ inches, (4) a 2 feet 1½ inches seam base at 987 feet, (5) a 2 feet 8½ inches seam base at 1,479 feet 1½ inches, (6) a 7 feet seam base at 1,533 feet 5½ inches and (7) a 5 feet 5½ inches seam base at 1,997 feet 9 inches. These seams, which total 25 feet 9 inches in thickness, are being analysed in detail by the National Coal Board. A good correlation exists between the two boreholes, the measures from 751 feet 3 inches (228.98 m) to 1,130 feet 6 inches (344.28 m) in the Steeple Aston Borehole being correlated with the Burford Coal Group which occurs between 1,475 feet (449.28 m) and 1,928 feet 5 inches (587.78 m) in the Apley Barn Borehole, the measures from 1,130 feet 6 inches (344.28 m) to 1,393 feet 3 inches (424.36 m) being correlated with the Crawley Group at 1,928 feet 5 inches (587.78 m) to 2,600 feet (792.48 m) in Apley Barn, the measures from 1,393 feet 3 inches (424.36 m) to 1,533 feet 5½ inches (467.40 m) with the Witney Coal Group at 2,600 feet (792.48 m) to 2,872 feet 4 inches (875.49 m) in Apley Barn and the measures from 1,533 feet 5½ inches (467.40 m) to 2,003 feet 6 inches (610.67 m) with the Arenaceous Coal Group at 2,872 feet 4 inches (875.49 m) to 3,968 feet 7 inches (1,209.62 m) in the Apley Barn Borehole². Farther afield the Burford Coal Group correlates with the Radstock Group of the Somerset Coalfield, the Witney Coal Group with part of the Farrington Group of Somerset and the Arenaceous Coal Group with the Mangotsfield Group of Somerset and the

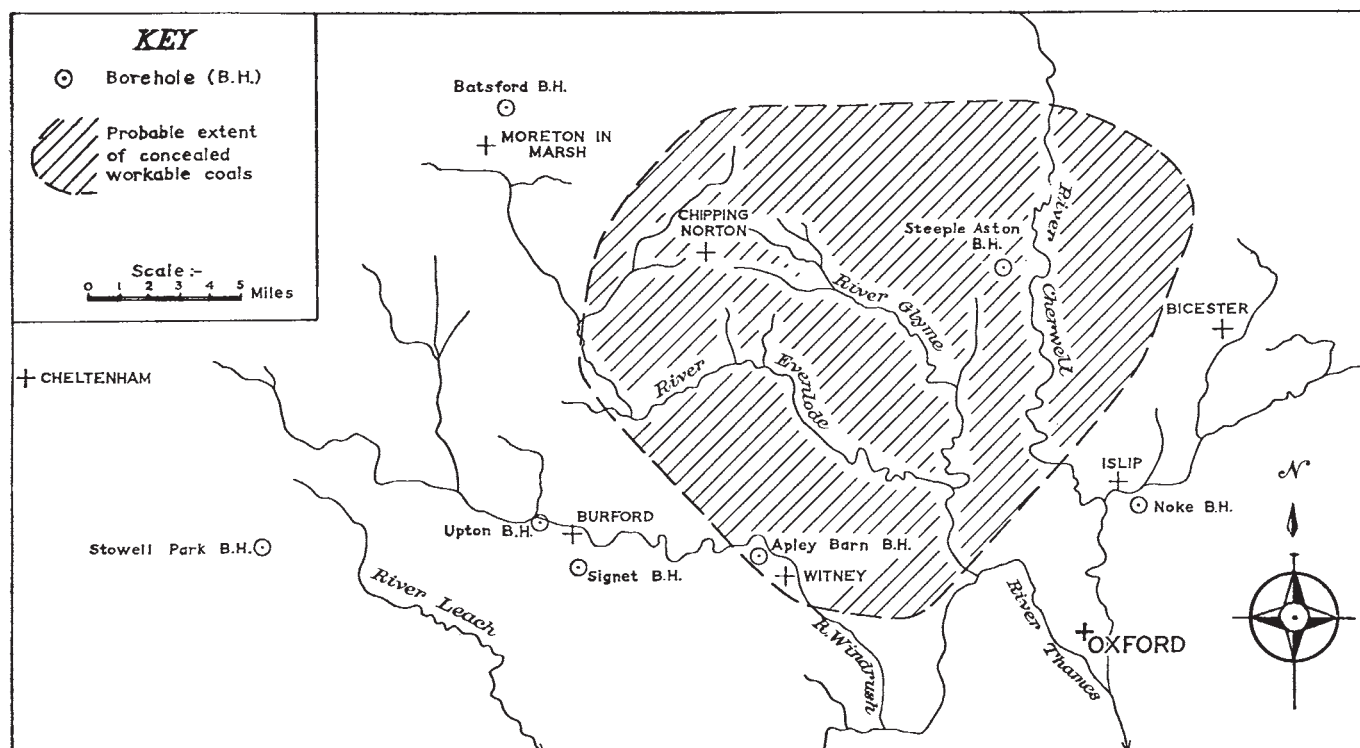


Fig. 1 Probable area of concealed workable coal in Oxfordshire.

upper part of the Pennant Group of the Forest of Dean Coalfield².

In the Apley Barn Borehole, the Upper Coal Measures rested unconformably on Upper Devonian sandstones, conglomerates and red and green mudstones but in the Steeple Aston Borehole a thick suite of basic intrusive rocks and agglomerates occurred beneath the Arenaceous Coal Group at 2,003 feet 6 inches (610.67 m) down to 2,545 feet 4 inches (775.82 m). Below these rocks a unique sequence of Upper Devonian marine and estuarine sediments was proved down to 3,172 feet 3 inches (966.90 m). These beds, which are yielding highly significant palynological and palaeontological results, are intruded by six thin basalt sills and the borehole was terminated in yet another basalt intrusion at 3,199 feet 3 inches (975.13 m). Natural gas was encountered in some of the sandstones of the Arenaceous Coal Group and the Devonian which was almost certainly produced by the thermal metamorphism of these carbonaceous formations. If the intrusions are of widespread lateral extent then it is possible that a small gas field may exist in the vicinity of the borehole; this would have to be proved by further drilling and pumping tests.

The probable area of concealed workable coals is shown in Fig. 1. The absolute northern limit is unknown but it almost certainly does not reach as far as Banbury, where the gravity anomaly map shows igneous or dense basement rocks at a comparatively shallow depth. Similarly it does not extend as far to the south-east as the Noke³ Borehole (some 5 miles north-east of Oxford) where Upper Old Red Sandstone underlies Mesozoic rocks at a depth of only 380 feet (115.82 m). The north-easterly limit is very uncertain and might well extend some distance beyond Bicester. The Apley Barn and Upton⁴ boreholes effectively prove the southerly and south-westerly limits of working on grounds of depth of burial. The absolute westerly limit is undetermined, but to the north-west the Batsford Borehole⁵ proved 524 feet 6 inches (159.87 m) of Upper Coal Measures but no workable seams. Thus the estimated total area where workable seams may reasonably be expected to occur may be as great as 200 to 250 square miles and may contain some 6,000 million tons of coal. The apparent dip in the Upper Coal Measures in both the Apley Barn and Steeple Aston Boreholes was low (3° to 4°) and the area is

probably one of simple structure. It should be emphasized, however, that the seams are thin, probably uneconomic at the present time, and that a great deal of further exploration would be necessary before a working colliery could be established in the area.

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Received July 9, 1971.

¹ Stubblefield, C. J., and Trotter, F. M., *Nature*, **191**, 953 (1961).

² Poole, E. G., *Bull. Geol. Surv. Great Brit.*, **29**, 1 (1969).

³ Falcon, N. L., and Tarrant, L. H., *Quart. J. Geol. Soc.*, **106**, 141 (1951).

⁴ Worssam, B. C., *Bull. Geol. Surv. Great Brit.*, **20**, 107 (1963).

⁵ Strahan, A., *Sum. Prog. Geol. Surv.*, **1912**, 90 (1913).

Formation of 2,3,7,8-Tetrachlorodibenzodioxin by Thermal Decomposition of Sodium 2,4,5-Trichlorophenate

IN the course of investigating an explosion which occurred in the Coalite Company's 2,4,5-trichlorophenol plant in 1968, a white crystalline solid of high melting point and extremely high toxicity was isolated which proved to be 2,3,7,8-tetrachlorodibenzodioxin. The manufacture of 2,4,5-trichlorophenol involves the hydrolysis of 1,2,4,5-tetrachlorobenzene using methanol and caustic soda at elevated pressure or ethylene glycol and caustic soda at atmospheric pressure. The plant in which the accident occurred used the latter process.

Small scale experiments in which 1,2,4,5-tetrachlorobenzene hydrolysates were allowed to heat up to higher temperatures than the normal 180° C showed a significant exothermic reaction after residual ethylene glycol had distilled off. Hydro-

lysates of all isomers of trichlorobenzene and mixtures of caustic soda and ethylene glycol all had the exothermic reaction in common starting in the 230° C region and proceeding rapidly and uncontrollably to around 410° C. This exotherm, which we attributed to the decomposition of sodium 2-hydroxyethoxide ($\text{NaOCH}_2\text{CH}_2\text{OH}$), was invariably accompanied by a huge volume of white vapours. Full analyses of the evolved gases were never possible although the presence in trace amounts of ethylene oxide was established. In the course of one such exothermic reaction of a 1,2,4,5-tetrachlorobenzene, distillate was collected which contained the usual di, tri and higher ethylene glycols and a white microcrystalline solid, melting point 298°–300° C, of elemental analysis 43.93%, 1.88% H, 36.70% Cl with the residue oxygen; this was designated C8.

A small sample of C8 recrystallized from benzene was examined by spectroscopic and gas liquid chromatographic techniques. Mass spectrographic studies of pure C8 and an authentic sample of 2,3,7,8-tetrachlorodibenzodioxin showed them to have identical fragmentation patterns, and the former to have molecular weight 322. The nuclear magnetic resonance spectrum of C8 showed one singlet proton signal at $\tau=3.7$; no response was observed in the aliphatic region of the spectrum; this is consistent with the symmetrical structure of 2,3,7,8-tetrachlorodibenzodioxin. Gas liquid chromatographic traces of authentic 2,3,7,8-tetrachlorodibenzodioxin and C8 run in precisely the same conditions gave single peaks of the same retention time. On this evidence it was concluded that purified C8 and 2,3,7,8-tetrachlorodibenzodioxin were identical and the elemental analysis quoted earlier which corresponded more closely to $\text{C}_{14}\text{H}_7\text{Cl}_4\text{O}_4$ than the required $\text{C}_{12}\text{H}_4\text{Cl}_4\text{O}_2$ reflected its relative lack of purity.

The high toxicity and chloracne effects of 2,3,7,8-tetrachlorodibenzodioxin have been previously reported^{1–6}; checks were therefore made on C8 using rabbits. Single oral doses of 1 or 10 $\mu\text{g}/\text{kg}$ were given to the animals; the higher dose level killed them all, and the lower dose caused serious liver damage and chloracne. This demonstrates the exceptional toxicity of this material.

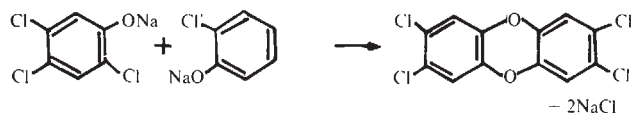


Fig. 1

The 2,3,7,8-tetrachlorodibenzodioxin (dioxin) was formed by mutual reaction of sodium 2,4,5-trichlorophenolate molecules (Fig. 1) under the influence of the highly exothermic decomposition of sodium 2-hydroxyethoxide and sublimed from the reaction mixture. In preparative experiments using this method, very low yields of dioxin were isolated, chiefly because of its low tendency to sublime, but there is strong evidence of its presence in the residue after thermal decomposition. For example 218 g hydrolysate (containing 91 g of sodium 2,4,5-trichlorophenolate) with a dioxin content of 17 p.p.m. was heated at 230°–260° C for 2 h, and gave a sublimate of only 6.4 mg dioxin, but the residue had a dioxin content of 1,600 p.p.m. Heating 1,2,4,5-tetrachlorobenzene hydrolysates at 180° C (normal reaction temperature) even for prolonged times gave only minimal dioxin contents.

Experiments on the thermal decomposition of hydrolysate of 1,2,3-, 1,2,4-, and 1,3,5-trichlorobenzenes (which collectively contained all six isomers of dichlorophenols), in identical conditions to those which produced C8, while undergoing exothermic reactions gave no visible or gas liquid chromatographic evidence of lower chlorinated dioxins. Distillates and residues formed in these thermal decompositions when tested for toxicity and chloracne on rabbits showed no harmful

effects at all at doses as high as 1 g/kg. It is reasonable to conclude that in these conditions no lower chlorodioxins are formed.

A practical outcome of the isolation of the highly toxic dioxin was the development of a gas liquid chromatographic technique of analysis and monitoring of dioxin at all stages of 2,4,5-trichlorophenol manufacture. A revised reaction scheme minimizing the dioxin content of the product was worked out for a new 2,4,5-trichlorophenol plant which was commissioned in late 1969, and the safest possible method devised to dispose of dioxin contaminated residues. Currently produced 2,4,5-trichlorophenol contains <1 p.p.m. dioxin.

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- ¹ Bauer, H., Schultz, K. H., and Spiegelberg, U., *Arch. Gowerbepath. Gowerbehyg.*, **18**, 538 (1961).
- ² Farquharson, M. D., Gage, J. C., and Northover, J., *Brit. J. Pharmacol. Chemother.*, **13**, 20 (1957).
- ³ Hofmann, H. Th., *Arch. Exp. Pathol. Pharmacol.*, **232**, 228 (1957).
- ⁴ Jones, E. L., and Krizek, H., *J. Invest. Derm.*, **39**, 511 (1962).
- ⁵ Kimmig, J., and Schultz, K. H., *Dermatologica*, **115**, 540 (1957).
- ⁶ Higginbotham, G. K., Huang, A., Firestone, D., Verrett, J., Ress, J., and Campbell, A. D., *Nature*, **220**, 702 (1968).

BIOLOGICAL SCIENCES

Identification of Primate Sexual Pheromones and the Properties of Synthetic Attractants

OLFACTORY communication is now known to be important in determining the interaction between the sexes in a microsmatic higher primate, namely, the rhesus monkey^{1,2}. Vaginal secretions of ovariectomized, oestrogen-treated female rhesus monkeys contain "copulins" that stimulate the mounting activity and ejaculatory behaviour of male rhesus monkeys³. The behavioural effects of these secretions were blocked in males made temporarily anosmic, but became apparent when olfactory acuity had been restored; they thus seem to possess the properties of olfactorily acting pheromones. We have therefore investigated the chemical nature of these sex attractants.

Behaviourally active constituents of vaginal secretions can be extracted into ether⁴. A solution prepared by washing ether extracts with N/100 sodium hydroxide, acidifying the alkaline layer and re-extracting into ether, retained behavioural activity: results which suggest that these active constituents were acidic. We report here the further fractionation of vaginal secretions by chromatography on the anion-exchanger, diethylaminoethyl (DEAE)-cellulose, and on the identification of behaviourally active constituents by gas chromatography and mass spectrometry. To confirm our results, we made a synthetic mixture of authentic compounds and tested it on ovariectomized rhesus monkeys for its capacity to attract and stimulate males.

Procedures for testing the behavioural activity of samples have been described previously³. Essentially, tests consisted of applying a sample directly to the sexual skin of ovariectomized, untreated female rhesus monkeys. These had been ovariectomized at least 6 months before and were unreceptive to males which generally showed little sexual activity with such females. Samples were applied to these females immediately before behavioural tests with active males, each test lasting 1 h,

during which animals were observed from behind one way vision mirrors. Sixty-six tests were conducted with four pairs of animals and changes in the interactions of the pair were measured and filmed using behavioural criteria described before^{5,6}. Particular attention is given here to changes in the numbers of attempts at mounting of females by males and to the changes occurring in the numbers of ejaculations. Two further ovariectomized rhesus monkeys, each receiving 10 µg oestradiol monobenzoate subcutaneously daily, were used to provide a source of secretions: these were collected twice daily by lavage with a vaginal pipette using 1 ml. distilled water and were immediately extracted into 2 ml. of diethyl ether. A pool of forty extracts was washed with 5 ml. N/100 sodium hydroxide, titrated to pH 7.4 and eluted through a column of DEAE-cellulose (Whatman DE-52) with 50 mM (pH 7.4) sodium phosphate buffer. The eluate was automatically collected into fractions which were then combined according to their elution volume relative to that of a phenolic component, detected by continuous monitoring for ultraviolet absorbance at 280 nm (Fig. 1), and now identified as *p*-hydroxyphenylpropionic acid (HPPA). Fractions were acidified, extracted into ether, and tested for behavioural activity. That corresponding to 30–50% of the elution volume of HPPA was found to be highly active (Fig. 2A). The number of attempts at mounting females made by the two males increased from six during twelve pre-treatment tests, when ether was applied for control purposes, to fifty-two during twelve treatment tests when the fraction was applied (χ^2 test, $P < 0.01$): there were no ejaculations during the pre-treatment period compared with twelve during treatment (χ^2 test, $P < 0.001$).

Ether extracts of the behaviourally active 30–50% fraction were further examined by analytical gas chromatography using 'Carbowax 20M'-terephthalic acid columns in Pye 104 and Perkin-Elmer F 11 gas chromatographs. The retention times of the five most volatile components, 86, 131, 152, 203 and 251 U, were compared with those of the following acids: acetic (87 U), propionic (131 U), *iso*-butyric (152 U), *n*-butyric (203 U), *iso*-valeric (251 U). A synthetic mixture of these acids co-injected with an equal volume of the natural extract showed no separation between the two mixtures. Confirmation of the identity of the five components was obtained by preparative gas chromatography and mass spectrometry. Five aliquots (2 µl. each) of the active ether extract were separately injected onto the same column fitted with a preparative attachment (10/1 effluent split). The effluent corresponding to each of the five peaks was collected individually in melting point U-tubes at -70°C : these were cut and installed in the direct insertion probe of an AEI-MS 9 mass spectrometer. The resultant mass

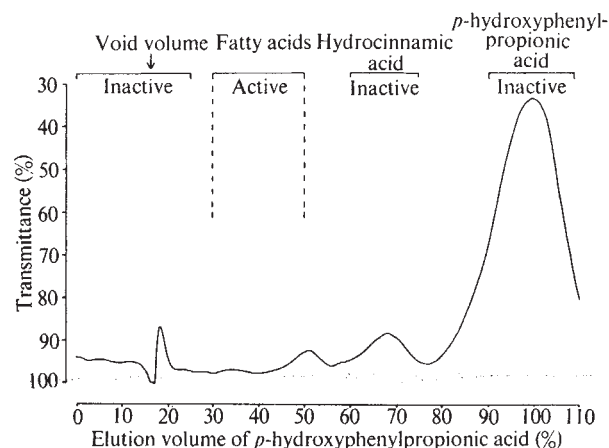


Fig. 1 Elution profile at 280 nm on DEAE-cellulose of alkaline re-extracts of vaginal secretions from ovariectomized, oestrogen-treated rhesus monkeys. The fractions were tested for behavioural activity; that containing fatty acids was found to be active, and was subjected to further analysis by gas chromatography and mass spectrometry.

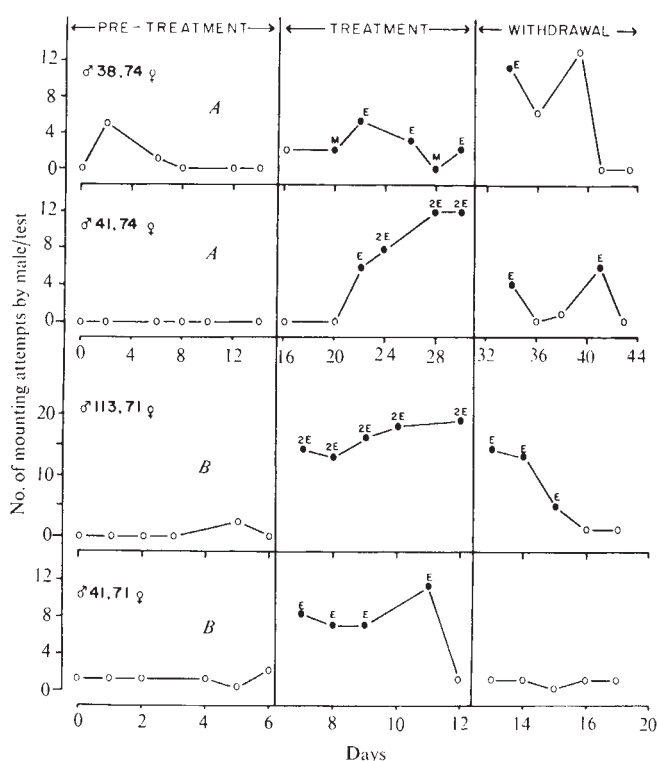


Fig. 2 Sexual stimulation of male rhesus monkeys by: A, the 30–50% fraction of vaginal secretions separated on a DEAE-cellulose column as indicated in Fig. 1; B, a synthetic mixture of the five short-chain fatty acids specified in the text.

spectra were compared with those of authentic samples obtained in the same way to avoid differences resulting from the presence of solvent or column impurities. These spectra established the identification of the five volatile constituents of the active fraction.

To ascertain if the five aliphatic acids in the behaviourally active fraction were responsible for its sex attractant properties, a mixture of authentic acids was made up to match the concentrations present in a pool of twenty-four washings collected from three ovariectomized females treated with oestrogen. The synthetic mixture contained 9.2 µg acetic, 8.8 µg propionic, 4.2 µg *iso*-butyric, 12.8 µg *n*-butyric and 8.3 µg *iso*-valeric acids/ml. of ether. A 2 ml. sample of this mixture, containing about 1.5 times the acid content of a single vaginal washing, was applied to the sexual skin of each of two ovariectomized females and tested for behavioural activity (Fig. 2B). The number of mounting attempts made by the two males increased from eight during twelve pre-treatment tests, when ether was applied for control purposes, to 114 during ten tests when applications of the synthetic mixture were made (t test, $P < 0.001$): there were no ejaculations during the pre-treatment period compared with fourteen during treatment (χ^2 test, $P < 0.001$). The persistence of mounting and ejaculation in some tests after withdrawing treatment was attributed to the influence of a recently rewarding sexual experience which exerted a reinforcing effect on subsequent behaviour⁴.

The identification of these volatile aliphatic acids as naturally occurring constituents of vaginal secretions in the rhesus monkey, and the demonstration that a synthetic mixture of authentic acids possesses equally powerful sex attractant properties, together provide strong evidence that the attractant properties of oestrogen-stimulated vaginal secretions depend, at least in part, on their acid content. This view is strengthened by the absence of acids, or their presence in very low concentrations, in the secretions of ovariectomized, untreated females⁷. We have already established that the behavioural effects of the unfractionated, parent sections are mediated by olfaction¹, so

we assume that fractions of these secretions act similarly. These findings identify and chemically characterize male sex attractants produced by a female primate, but this in no way precludes the existence of other unidentified substances with related effects. Their production by other than vaginal sources—for example, the glands of the skin—is currently being investigated.

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- ¹ Michael, R. P., and Keverne, E. B., *Nature*, **218**, 746 (1968).
- ² Michael, R. P., in *Recent Advances in Primatology*, 1 (edit. by Carpenter, C. R.) (S. Karger, Basel, 1969).
- ³ Michael, R. P., and Keverne, E. B., *Nature*, **225**, 84 (1970).
- ⁴ Keverne, E. B., and Michael, R. P., *J. Endocrinol.* (in the press).
- ⁵ Michael, R. P., and Saayman, G. S., *J. Endocrinol.*, **41**, 231 (1968).
- ⁶ Michael, R. P., and Welegalla, J., *J. Endocrinol.*, **41**, 407 (1968).
- ⁷ Michael, R. P., Keverne, E. B., and Bonsall, R. W., *Science*, **172**, 964 (1971).

***p*-Chlorophenylalanine and Copulatory Behaviour in the Male Rat**

EVIDENCE has accumulated that copulatory behaviour in the female and male rat is inhibited by increased central nervous serotonergic tone¹⁻⁴. One approach to the study of the specificity of the antagonistic relationship between serotonin and copulatory behaviour has been selectively to increase serotonin by the combination of a monoamine oxidase inhibitor and the serotonin precursor 5-hydroxytryptophan (5-HTP). B. J. M. has shown that this treatment inhibits the copulatory response (lordosis reflex) in the female rat⁴ and we have also shown⁵ it to decrease the number of male rats mounting oestrous females. Analogous experiments with the catecholamine precursor dihydroxyphenylalanine (DOPA) revealed no inhibitory effect of increased catecholamine concentrations. According to the studies of Shillito^{5,6} and Tagliamonte *et al.*⁷, a selective decrease of serotonin by the serotonin synthesis inhibitor *p*-chlorophenylalanine⁸ augmented sexual and social interaction between male rats, and in our work this agent also facilitated sexual receptivity in oestrogen-treated ovariectomized females⁹. Increased copulatory behaviour after *p*-chlorophenylalanine treatment has recently been shown in the male and female cat^{10,11}, although contradictory results are also available¹²⁻¹⁴. The purpose of the experiments described here was to study the effect of *p*-chlorophenylalanine on heterosexual mounting behaviour in castrated males, which had been given a dose of testosterone adjusted to maintain a submaximal mounting response.

The subjects were 140 male Wistar rats (350–420 g, specific pathogen free, Møllegaard, Ejby, Denmark) castrated as adults and with proven sexual experience before castration. Copu-

latory tests took place during the dark period of a reversed day–night cycle (11 h dimmed light, 13 h bright light). The male was allowed 5 min of adaptation in the test cage before a receptive female (spayed female treated with 50 µg of oestradiol benzoate 53 h before the test and 1 mg of progesterone 5 h before the test) was introduced. The time allowed from the introduction of the female to the first mount was restricted to 3 min. If the male mounted within 3 min the test continued for another 3 min or until ejaculation had occurred. In this account we are concerned chiefly with the readiness of the males to mount. Tests were carried out regularly once a week throughout the investigation.

Three to five weeks after castration the number of animals which mounted the receptive female had decreased to about 50%. After less than 50% of a batch of animals had mounted the female in two consecutive weekly tests, testosterone propionate was given to the whole of the batch. Treatment was once a week and the animals were tested 3 or 4 days after the hormone treatment. The dose (0.14–0.20 mg kg⁻¹ given subcutaneously) was adjusted to give a submaximal response as to the number of males with mounting behaviour within the 3 min observation period. After the response rates at the weekly tests had become stable, the main experiment began.

The experimental group was given a neuropharmacological agent and a control group received a blank solution: this was our “experimental test”. As a comparison, the last no-drug test—the “pre-experimental test”—was used.

DL-*p*-Chlorophenylalanine methylester HCl (PCPA), 100 mg kg⁻¹, was given intraperitoneally for 4 days and the animals were tested 6 h after the last injection. There was a significant increase in the number of animals which mounted the female and also the number of mounts performed each minute (Table 1A). By giving more testosterone, the response rate was increased to about 70–80% of males mounting, and the stimulatory effect of PCPA on the readiness to mount a receptive female was no longer obvious (Table 2). If the subject was retested after 0.5–1 h, however, this time with a castrated male introduced instead of a receptive female, there was a significant increase in mounting behaviour compared with animals not treated with PCPA. Previously¹³ no stimulatory effect was seen on the heterosexual copulatory behaviour of intact vigorous males after PCPA treatment, but rather an effect on the mounting of intact males by intact males⁵⁻⁷. Our data indicate that the stimulatory effect of PCPA on male copulatory behaviour is only visible if the males are on a testosterone treatment which is submaximal as to activation of mounting behaviour. The fact that it was still possible to detect an effect when a male instead of a female was used as mounting partner might be a result of the fact that the male was less of an incentive as a mounting object.

To test whether the augmented mounting response could be attributable to a non-specific increase in exploratory behaviour, locomotor activity was measured by an ‘Animex’ activity meter (Farad Electronics, Hägersten, Stockholm). Movement of the animals across a tuned oscillator coil system results in change of the tuning which is recorded as a count. One subject at a time was placed in the apparatus. Each recording lasted 10 min and was carried out 0.5–1 h after the copulation test (Table 1A, 1–2). PCPA treatment decreased spontaneous locomotor activity. To rule out the possibility that this result was caused by fatigue after the test, another batch of six plus six animals was tested in the ‘Animex’ after the same drug treatment but without a copulation test and at the time at which the copulation test would have been performed. The result was very similar (Table 1A, 3–4). Thus, PCPA increased the number of males mounting and the number of mounts per minute, although the animals became sluggish in the locomotor test. This emphasizes the specificity of the augmenting effect of PCPA on the readiness of the male to mount a receptive female.

The effect of PCPA on copulatory behaviour was also investigated in twenty-six adrenalectomized males. All received

0.9% NaCl in their water bottles and once a week dexamethasone, 0.5 mg per animal, was given subcutaneously. Experimental animals were given PCPA intraperitoneally, 100 mg kg⁻¹ on the first day and 50 mg kg⁻¹ each day for another 3 consecutive days, and they were tested 6 h after the last injection. Compared with the pre-experimental test values and the saline-treated controls there was an obvious increase in the mounting performance of subjects treated with PCPA (Table 1B). This stimulatory effect on the readiness to mount a receptive female in castrated and adrenalectomized males rules out the possibility that PCPA increases the mounting rate by stimulating endogenous testosterone production. The number of mounts per minute (pre-experimental test) was less than in rats not adrenalectomized, probably because in spite of the dexamethasone treatment the animals became less alert after adrenalectomy. The limited number of subjects (three) which mounted both in the pre-experimental and experimental test makes it difficult to say whether there is a true increase in mounts per minute.

It has been demonstrated³ that the general increase of monoamine concentrations achieved by the monoamine oxidase inhibitor pargyline (40 mg kg⁻¹, given intraperitoneally) significantly inhibited mounting behaviour in males. This is confirmed in this study (Table 3A). We investigated the possible prevention of this inhibition by decreased biosynthesis of serotonin caused by PCPA. When the animals were pretreated with PCPA, 4 × 100 mg kg⁻¹, given intraperitoneally, the inhibitory effect of pargyline on the mounting behaviour was not obtained (Table 3B) (see *Note added in proof*). A comparison of the data in the experimental test with the results of the pre-experimental trial reveals that there was still an evident increase in the percentage of animals mounting. The increase in mounting was about the same as if pargyline had not been given (compare Table 1A). In contrast to animals treated only with PCPA, however, there was no significant change in the

number of mounts per minute. The inhibitory effect of PCPA on serotonin biosynthesis (tryptophan hydroxylase inhibition) does not involve the step from the precursor amino-acid 5-HTP to serotonin. Thus, by treating with 5-HTP it is possible to increase serotonin concentrations although PCPA has been given. DL-5-HTP was injected 30 min before the mating test in an otherwise analogous PCPA plus pargyline experiment, which gave a clearcut inhibitory effect on the copulatory behaviour (Table 3B, 2). Overt behaviour was no more affected in these animals than in those which had PCPA alone.

These data suggest that PCPA in the male rat increases the hormone-activated copulatory response. This effect is probably related to the ability of PCPA to decrease the serotonergic tone, although the possibility that PCPA interacts with further biochemical events which would contribute to its effect on copulatory behaviour cannot be excluded. In the female rat, the results of similar experiments led to the hypothesis that there are serotonergic pathways mediating inhibition of copulatory behaviour^{1,2,4,9,15}. It has been suggested that decreased serotonergic activity would remove this inhibition and thereby enhance the hormone-activated copulatory response. This hypothesis can be extended to male copulatory behaviour.

One may ask whether this inhibitory system is restricted to the sex-specific copulatory behaviour pattern or if female behaviour in the male and male behaviour in the female is under the same serotonergic control. Previous data suggest the latter: decreased monoamine concentrations achieved by amine depletors (reserpine and tetrabenazine) facilitate female copulatory behaviour (lordosis response) in oestrogen-treated males castrated as adults¹⁶. The specificity of serotonin in this respect needs further investigation, however.

We thank Miss Ann-Kristin Söderlund for technical assistance. Oestradiol benzoate and progesterone were donated by Pharmacia, Uppsala, Sweden; testosterone propionate by

Table 1 Effect of PCPA on Testosterone Propionate Activated Heterosexual Mounting Behaviour and Locomotor Activity for Castrated Male Rats

Treatment	Mounting (%)			Mounts per min *			Locomotor activity	
	Pre-experimental test	Experimental test	No.	Pre-experimental test	Experimental test	No. †	'Animex' activity meter counts per 10 min *	No.
A 1 PCPA, 4 × 100 mg kg ⁻¹ , i.p.	49	90	39	3.4 ± 0.3	5.1 ± 0.3 **	19	357 ± 33	12
2 Saline, 4 × 0.4 ml., i.p.	45	45	40	3.9 ± 0.3	3.5 ± 0.3 §	15	691 ± 24	12
3 PCPA, 4 × 100 mg kg ⁻¹ , i.p.	—†	—	—	—	—	—	336 ± 62	6
4 Saline, 4 × 0.4 ml., i.p.	—	—	—	—	—	—	916 ± 34	6
B Adrenalectomized animals								
1 PCPA, 100 + 3 × 50 mg kg ⁻¹ , i.p.	23	92 **	13	1.4 ± 0.3	3.1 ± 0.8 §	3		
2 Saline, 4 × 0.4 ml., i.p.	46	46	13	1.9 ± 0.4	2.5 ± 0.4 §	3		

* Mean ± s.e.

† The estimate of mounts per minute is based on subjects which mounted in both the pre-experimental and experimental tests.

‡ No copulatory test performed. *P* of difference in % of animals mounting between the pre-experimental and experimental tests was tested by the Sign test. Student's *t* test was used for mean difference in mounts per minute and to test the difference between PCPA and saline treatment on locomotor activity.

§ NS, *P* > 0.05. ** *P* < 0.01. || *P* < 0.001.

PCPA and saline were given once daily for 4 consecutive days. The last injection was given 6 h before the experimental test. Adrenalectomized animals received dexamethasone 0.5 mg per animal subcutaneously once a week.

Table 2 Effect of PCPA on Testosterone Propionate Activated Mounting of Female and of Male Partner, with Castrated Male Rats

Treatment	Mounting of female (%)		<i>P</i>	Mounting of male (%)		<i>P</i> †	No.
	Pre-experimental test	Experimental test *		Experimental test	<i>P</i> †		
PCPA, 4 × 100 mg kg ⁻¹ , i.p.	67	83	> 0.05	67	< 0.01		12
Saline, 4 × 0.4 ml., i.p.	75	83	> 0.05	17			12

PCPA and saline was given once a day for 4 consecutive days. The last injection was given 7 h before the first experimental test. The test for mounting a male was performed 0.5–1 h after the test for mounting a female.

* Difference between pre-experimental and experimental was tested by the Sign test.

† Difference between PCPA and saline treatment was tested by the χ^2 test.

Table 3 Effect of Pargyline Alone and in Combination with PCPA and PCPA + 5-HTP on Testosterone Propionate Activated Mounting

Treatment	Pre-experimental test	Mounting (%)		Mounts per minute*		No. †
		Experimental test	No.	Pre-experimental test	Experimental test	
A 1 Pargyline, 40 mg kg ⁻¹	78	6	18	1.8 ± 0.3	—	(14)
2 Saline, 0.4 ml.	76	82	17	3.0 ± 0.2	2.8 ± 0.4§	12
B 1 PCPA, 4 × 100 mg kg ⁻¹ and pargyline, 40 mg kg ⁻¹	38	75**	24	2.3 ± 0.5	3.1 ± 0.7§	
2 PCPA, 4 × 100 mg kg ⁻¹ and pargyline, 40 mg kg ⁻¹ and 5-HTP, 5.0 mg kg ⁻¹	50	4**	24	3.0 ± 0.5	—	(12)
3 Saline, 4 × 0.4 ml.	58	50	24	2.5 ± 0.4	3.2 ± 0.4	10

* Mean ± s.e. Castrated male rats were used.

† The estimate of mounts per minute is based on subjects which mounted in both the pre-experimental and experimental tests.

Other footnotes are as in Table 1.

P of difference was calculated as in Table 1. PCPA (B1,2) and saline (B3) were given once daily for 4 consecutive days. The last injection was given 10 h before the experimental test. Pargyline was injected 6 h and 5-HTP 0.5 h before the experimental test. All injections were given intraperitoneally.

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Note added in proof. After this paper had been submitted for publication, data on the effect of pargyline and pargyline + PCPA on the copulatory behaviour in the male rat were reported by A. Tagliamonte, P. Tagliamonte and G. L. Gessa (*Nature*, 230, 244; 1971). Their results are in good agreement with our earlier³ and present data.

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- ¹ Meyerson, B. J., *Acta Physiol. Scand.*, **63**, 241 (1964).
- ² Meyerson, B. J., *Ann. Med. Exp. Fenn.*, **46**, 394 (1968).
- ³ Malmnäs, C.-O., and Meyerson, B. J., *Acta Pharmacol. Toxicol.*, **28**, Suppl. 1 (1970).
- ⁴ Meyerson, B. J., *Arch. Intern. Pharmacodyn.*, **150**, 4 (1964).
- ⁵ Shillito, E. E., *Brit. J. Pharmacol.*, **36**, 193 (1969).
- ⁶ Shillito, E. E., *Brit. J. Pharmacol.*, **38**, 305 (1970).
- ⁷ Tagliamonte, A., Tagliamonte, P., Gessa, G. L., and Brodie, B. B., *Science*, **166**, 1433 (1969).
- ⁸ Koe, B. K., and Weissman, A., *J. Pharmacol. Exp. Ther.*, **154**, 499 (1966).
- ⁹ Meyerson, B. J., and Lewander, T., *Life Sci.*, **9**, 661 (1970).
- ¹⁰ Hoyland, V. J., Shillito, E. E., and Vogt, M., *Brit. J. Pharmacol.*, **40**, 659 (1970).
- ¹¹ Ferguson, J., Henriksen, S., Cohen, M., Mitchell, G., Barchas, J., and Dement, W., *Science*, **168**, 499 (1970).
- ¹² Segal, D. S., and Wahlen, R. E., *Psychopharmacologia*, **16**, 434 (1970).
- ¹³ Wahlen, R. E., and Luttge, W. G., *Science*, **169**, 1000 (1970).
- ¹⁴ Zitrin, A., Beach, F. A., Barchas, J. D., and Dement, W. C., *Science*, **170**, 868 (1970).
- ¹⁵ Meyerson, B. J., *Psychopharmacologia*, **6**, 210 (1964).
- ¹⁶ Meyerson, B. J., *Nature*, **217**, 683 (1968).

p-Chlorophenylalanine facilitates Copulatory Behaviour in Male Rats

It has been proposed that the inhibition of male copulatory patterns by anterior portions of the nervous system¹ is mediated by brain monoamines²⁻⁴, for reserpine facilitates certain aspects of the male pattern in rats³⁻⁵ although monoamine oxidase inhibitors retard copulatory behaviour (D. A. D., H. N. Davis and P. E. Jansen, results submitted for publication). Meyerson has proposed⁶ that an analogous mechanism may control female oestrous behaviour in rats.

These data suggest that *p*-chlorophenylalanine (PCPA), which depletes brain serotonin⁷, should facilitate male copulatory behaviour as it does female oestrous behaviour⁸. Evidence that this drug facilitates mounting behaviour in male rats^{2,9-12} supports this hypothesis. But another report¹³ indicates that the species typical copulatory pattern of male rats is not affected by PCPA. We have now demonstrated that PCPA can substantially facilitate the normal pattern of heterosexual behaviour in the male rat.

Twenty-three male Long-Evans rats 95 days old were pre-tested—each was handled, followed by two successful tests of copulatory behaviour. Twenty-eight females of the same age and strain served as partners. Tests were conducted in 'Plexiglas' arenas 76–86 cm in diameter and 61–66 cm high.

Each male received three experimental tests of copulatory behaviour at intervals of 4 weeks. Tests followed administration of isotonic saline, 50 mg kg⁻¹ or 100 mg kg⁻¹, of a saline suspension of DL-*p*-chlorophenylalanine (pH 1.8). Injections were given intraperitoneally on four successive nights between midnight and 0100 h and tests were initiated on the day after the fourth injection at 0300 h—5 h after the beginning of the dark phase of the light-dark cycle. Subgroups were tested in each of the six possible running orders in a balanced design.

The tests began with the introduction of a receptive female into the test arena 5 min after the introduction of the male, and were terminated after the first intromission following the third ejaculation by the male. Females were brought into behavioural oestrus with intramuscular injections of 0.1 mg of oestradiol benzoate 3 days before testing and 1.0 mg of progesterone approximately 3 h before testing. Only receptive females were used.

Copulatory behaviour in rats consists of bouts or series of mounts (without intromission) and vaginal intromissions, with each complete series terminated by an ejaculation. We considered the following standard measures: mount latency (ML)—the period from the introduction of the female to the first mount; intromission latency (IL)—the period until the first intromission; ejaculation latency (EL)—the period from the first intromission of a series to ejaculation; intromission frequency (IF)—the number of intromissions in a series; mount frequency (MF)—the number of mounts in a series; mean inter-intromission interval (MIII)—the mean interval separating the intromissions of a series; and post-ejaculatory interval (PEI)—latency from ejaculation to the next intromission. Individual series are designated by a hyphen and the appropriate number (for example, IF-3).

We used multivariate analyses of variance with repeated measures¹⁴ on our data. There was a significant overall effect of drug condition across series on all five measures characterizing series (EL, MIII, PEI, IF, MF). The mean scores and

Table 1 Mean Scores and Significance Levels of Male Copulatory Behaviour as a Function of Drug Condition

Measure	Saline	Mean score		Total	Significance level*		
		50 mg kg ⁻¹	100 mg kg ⁻¹		Saline versus 50 mg kg ⁻¹	Saline versus 100 mg kg ⁻¹	50 mg kg ⁻¹ versus 100 mg kg ⁻¹
Latency measures (s)							
ML	14.43	7.57	6.87	NS	NS	NS	NS
IL	47.30	10.30	12.35	NS	NS	NS	NS
EL-1	342.26	210.00	168.87	< 0.01	NS	< 0.05	NS
EL-2	170.65	98.65	98.09	< 0.01	< 0.05	< 0.01	NS
EL-3	248.65	109.09	125.13	< 0.05	(< 0.10)	(< 0.10)	NS
MIII-1	39.90	24.12	20.12	< 0.01	NS	< 0.05	NS
MIII-2	40.43	27.29	25.85	(< 0.10)	NS	(< 0.10)	NS
MIII-3	46.38	27.55	29.99	(< 0.10)	(< 0.10)	NS	NS
PEI-1	339.00	322.83	322.30	NS	NS	NS	NS
PEI-2	416.35	377.57	379.13	< 0.01	NS	< 0.01	NS
PEI-3	486.52	430.52	446.09	< 0.05	(< 0.10)	NS	NS
Frequency measures							
IF-1	8.87	8.74	8.78	NS	NS	NS	NS
IF-2	4.74	3.78	3.87	< 0.01	< 0.05	< 0.05	NS
IF-3	5.17	3.87	4.04	< 0.01	< 0.01	< 0.05	NS
MF-1	5.30	2.39	2.43	< 0.05	(< 0.10)	< 0.05	NS
MF-2	1.65	1.35	0.70	< 0.05	NS	(< 0.10)	NS
MF-3	3.61	1.65	1.30	< 0.05	NS	(< 0.10)	NS

* Overall tests with multivariate repeated measures analyses (d.f. = 2,21); multiple comparisons with Scheffé's tests (d.f. = 2,21). NS, Not significant.

significance levels for all the measures for individual series are presented in Table 1. It is evident that PCPA substantially facilitated most aspects of the copulatory pattern. The means of all measures for all series have consistent differences indicative of this facilitation. Many of these differences were significant at the 0.05 level or better. In several cases, changes in group means in the drug treatments were accompanied by changes in group variances; in general, the drug treatments produced decreases in variances, although there were exceptions to this trend. Ejaculations were usually attained sooner, and after fewer mounts and intromissions, than after saline administrations, and post-ejaculatory refractory periods were shorter. Both dose levels facilitated the behaviour at least to some extent, but there were more significant differences after administration of the higher dose.

The demonstration of a facilitation effect of PCPA on male rat heterosexual copulatory activity is consistent with its facilitation of mounting behaviour^{2,9-12}. The effects of PCPA on copulatory behaviour of male cats are unclear^{15,16}. Our data are inconsistent with a study¹³ in which there was no effect of PCPA on heterosexual copulation in male rats. Differences between the two experiments which might account for our positive results include: our use of the reported^{2,12} optimal injection-test interval; our use of a larger number of subjects; our confinement of tests to a part of the photoperiod in which copulatory behaviour is relatively fast and variability relatively low¹⁷; our use of a balanced testing order with different subjects receiving treatment in all possible orders; and differences in the form and mode of injection of PCPA.

These data, together with others from our laboratory^{3,4}, are consistent with the hypothesis that brain monoamines, and particularly serotonin, inhibit male copulatory behaviour.

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- ¹ Beach, F. A., *Physiol. Rev.*, **47**, 289 (1967).
- ² Tagliamonte, A., Tagliamonte, P., Gessa, G. L., and Brodie, B. B., *Science*, **166**, 1433 (1969).
- ³ Dewsbury, D. A., and Davis, H. N., *Physiol. Behav.*, **5**, 1331 (1970).
- ⁴ Dewsbury, D. A., *Psychon. Sci.*, **22**, 177 (1971).
- ⁵ Soulaire, A., and Soulaire, M. L., *CR Soc. Biol.*, **155**, 1010 (1961).
- ⁶ Meyerson, B. J., *Acta Physiol. Scand., Suppl.*, **63**, 241 (1964).
- ⁷ Koe, B. K., and Weissman, A., *J. Pharmacol. Exp. Ther.*, **154**, 499 (1966).
- ⁸ Meyerson, B. J., and Lewander, T., *Life Sci.*, **9**, 661 (1970).
- ⁹ Gessa, G. L., *Ann. Internal Med.*, **73**, 622 (1970).
- ¹⁰ Gessa, G. L., Tagliamonte, A., Tagliamonte, P., and Brodie, B. B., *Nature*, **227**, 616 (1970).
- ¹¹ Shillito, E. E., *Brit. J. Pharmacol.*, **38**, 305 (1970).
- ¹² Sheard, M. H., *Brain Res.*, **15**, 524 (1969).
- ¹³ Whalen, R. E., and Luttge, W. G., *Science*, **169**, 1000 (1970).
- ¹⁴ Morrison, D. F., *Multivariate Statistical Methods* (McGraw-Hill, New York, 1967).
- ¹⁵ Ferguson, J., Henriksen, S., Cohen, H., Mitchell, G., Barchas, J., and Dement, W., *Science*, **168**, 499 (1970).
- ¹⁶ Zitrin, A., Beach, F. A., Barchas, J. D., and Dement, W. C., *Science*, **170**, 868 (1970).
- ¹⁷ Dewsbury, D. A., *Commun. Behav. Biol.*, **1**, 373 (1968).

Mate-seeking by Female *Amblyomma maculatum* (Acarina : Ixodidae) on a Bovine

LITTLE information is available concerning the attraction between sexes of ticks, and the literature contains no reports of sex pheromones in these arachnids. In some tick species the males are known to seek the attached females¹⁻⁴, though male bont ticks, *Amblyomma hebraeum* Koch, in Africa probably attract females⁵. When, however, I investigated the mating behaviour of the Gulf Coast tick, *Amblyomma maculatum* Koch, on bovines restrained inside environmentally controlled stalls (24 ± 3° C; 70 ± 7% relative humidity; 12 h photophase: 12 h scotophase per 24 h photocycle), I found that the females were attracted to the males.

In preliminary tests, female *A. maculatum* (AM) did not attach to a bovine, either alone, or in the presence of males of another species in the same genus (*Amblyomma americanum* (L.) (AA)). This effect is unusual because females of other tick species do attach to hosts in the absence of males⁶⁻⁸.

Therefore, in three replicates, stanchioned bovines were fitted with mating chambers (sleeves)⁹ and infested with ten ticks of each sex in the following combinations on the indicated day (counting day 1 as the time of first infestation): (1) AA males on day 1 and AM females on day 6; (2) AA males and AM females both on day 1; (3) AM females on day 1; (4) AM males on day 1 and AM females on day 6; (5) AM males and AM females both on day 1.

After the scheduled infestation was complete, the sleeves were inspected every 24 h for 8 days (counting from the day of infestation with females), and the number of attached AM females was recorded. Attachment of all ten females occurred only in sleeves that contained the AM males (treatments 4 and 5; Table 1), and 100% attachment of females occurred 5 days sooner in sleeves that contained already-attached AM males (treatment 4) than in sleeves that received the AM females and AM males at the same time (treatment 5). Apparently the males must feed for several days before most females will attach. Few females introduced into sleeves without males were stimulated to attach, and those that did attach remained no longer than 24 or 48 h. Rates of attachment of females in sleeves containing AA males were intermediate between those of females in sleeves with males of the same species and those of females in sleeves without males. Possibly the presence *per se* of the males or an interspecific pheromone induced moderate attachment of AM females in sleeves with AA males.

Table 1 Rates of Attachment to Bovines of AM ♀♀ placed Inside Sleeves Alone or with One of Four Groups of ♂♂

Treatment No.	AM ♀♀ placed inside sleeves	Replicate No.	No. AM ♀♀ attached at indicated day post infestation							
			1	2	3	4	5	6	7	8
1	With previously attached AA ♂♂	1	0	1	0	0	0	1	0	0
		2	1	1	0	1	3	2	8	7
		3	1	3	1	4	4	4	2	3
2	At the same time as AA ♂♂	1	0	0	0	0	0	0	0	1
		2	0	0	2	0	0	1	0	2
		3	1	0	2	4	3	4	6	4
3	Alone	1	0	0	0	0	0	0	1	0
		2	0	1	0	0	0	0	0	0
		3	0	1	0	0	0	2	3	1
4	With previously attached AM ♂♂	1	9	10*	10	10	10	10	10	10
		2	10	10	10*	10	10	10	10†	9
		3	8	10	10*	10	10	10	10†	9
5	At the same time as AM ♂♂	1	0	1	3	6	8	10	10	10*
		2	2	3	10	9	6	6	10	10*
		3	0	0	5	9	10	10	10	10

Each sleeve contained ten ticks of each sex.

* First mating observed.

† First detachment of mated, engorged females observed.

The females that attached in sleeves containing attached AM males (treatment 5) were mated beginning 2 or 3 days after the females were introduced, and detached when replete. Females introduced into sleeves at the same time as AM males (treatment 4), however, were not mated until 8 days post-infestation, because the completion of spermatogenesis by many male ixodid species does not take place until after they feed¹. Females released into sleeves containing conspecific males engorged partially were mated by the males, and eventually detached when replete. Females that attached in sleeves by themselves (treatment 3) or in sleeves with AA males (treatments 1 and 2) imbibed no discernible amounts of blood, and cross-mating did not occur between AA males and AM females.

Because each AM female that was introduced into a sleeve containing attached AM males actively sought the site of the male and attached immediately adjacent to it, the behaviour of AM females in seeking AM males was studied further in another test in which the two sexes were not confined in close

proximity. The methods were similar to those used in a study of the migration of AA males to AA females on bovines⁴ except that the AM females, not the males, were marked and released.

Each AM female was marked on the dorsum with 1 µl. of saturated acetone solutions of fluorescent powders (Series A pigments; Day-Glo Color Division, Switzer Bros., Inc., Cleveland, Ohio). Four days before the marked females were to be released on stanchioned bovines, the animals were infested with seventy-five AM males which were confined on an area of the upper shoulder by the stockinette-sleeve technique⁴. After 4 days, the sleeve was removed, and twenty-five females were released onto each of three areas (the hocks of one front and one hind leg, and the belly of the animal) on the sides of the animals opposite the sides on which the males were attached. Each group of twenty-five females was marked with a different colour for each site of release. Many females did not cling firmly to the hair of the animals and fell to the floor of the stall immediately after release and were subsequently lost.

At 24 h after release, the marked females were located on the animals with a portable ultraviolet lamp, and the site of attachment of each tick was recorded on a diagram of the animal. For a further 11 days, the cattle were inspected daily for paired adult ticks. Females found within 1 cm of a male were removed, examined under the ultraviolet lamp, and then discarded. I was therefore able to determine how long the females were on the hosts before they located the males. The test was replicated six times.

By 24 h after release, eighty of the ninety-two detected females had preferred to attach within 1 cm of males rather than attach at any other site on the animals' bodies; the second most preferred site of attachment (eight out of ninety-two) was the ears, even though no males were present in them. Thus, most females located males within 24 h regardless of the site of initial infestation (the last female took 10 days to reach the males). Of a total of 450 marked females originally released on the animals, 111 (25%) were paired with males when collected.

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- Balashov, Y. S., *Dokl. Akad. Nauk SSSR*, **110**, 1113 (1956).
- Arthur, D. R., *Ticks and Disease* (Row, Peterson and Co., Evanston, Illinois, and Elmsford, New York, 1962).
- Sactor, B., Hutchinson, M., and Granett, P., *J. Econ. Entomol.*, **41**, 296 (1948).
- Gladney, W. J., and Drummond, R. O., *J. Econ. Entomol.*, **63**, 1214 (1970).
- Lounsbury, C. P., *Agr. J. Cape Good Hope*, **15**, 728 (1899).
- Gladney, W. J., Drummond, R. O., Whetstone, T. M., and Ernst, S. E., *J. Med. Entomol.*, **7**, 92 (1970).
- Pervomaiskii, G. S., *Tr. Vses. Entomol. Obshchestva*, **44**, 62 (1954).
- Srivastava, S. C., and Varma, M. G. R., *J. Med. Entomol.*, **1**, 154 (1964).
- Gladney, W. J., and Drummond, R. O., *Ann. Entomol. Soc. Amer.*, **63**, 1036 (1970).

Systemic Action of an Insect Feeding Deterrent

MANY phytophagous insects are restricted in host range because of the presence of naturally occurring distasteful chemical substances in otherwise acceptable plants^{1,2}. In the

search for possible substitutes for toxic pesticides, however, comparatively little attention has been directed towards the application of non-toxic antifeeding compounds or rejectants as a means of deterring insects from attacking crops. To be of practical value, a rejectant should not only be persistent but also absorbed and translocated to the growing points of treated plants. Otherwise the new plant growth developing after treatment, being uncontaminated, will be selectively attacked while the older treated leaves remain distasteful.

The neem tree *Azadirachta indica* has many uses, one of which is that a suspension of crushed seeds or leaves will deter some insect species from feeding when applied directly to plant foliage or stored products. A compound which is a potent rejectant for the desert locust, *Schistocerca gregaria* Forsk.^{3,4}, has been isolated from seeds and termed azadirachtin⁵ though its structure has yet to be elucidated. We have now obtained results which show that azadirachtin, and possibly other substances present in neem extracts, can be absorbed by the roots and translocated within bean plants to act as a systemic rejectant.

Three products were tested against *Schistocerca* adults. These were (1) azadirachtin, the pure chemical; (2) an alcoholic concentrate, refined from a 95% ethanol extract of neem seed, containing 3.8% by weight of the seed; and (3) an aqueous suspension prepared by grinding seed kernels in water until the material passed through a 100-mesh sieve.

These products were diluted with water containing 0.05% 'Teepol' and applied in a range of seven concentrations to the soil around young bean plants at the six to eight leaf stage. The bean plants were transplanted singly to plastic cups containing 150 g of a soil consisting of a sieved and sterilized mixture of 3 parts loam, 2 parts sand and 1 part peat, and the different treatments were applied in 10 ml. as part of the first watering. The efficacy and persistence of the treatments were assayed by placing the treated plants, together with controls, randomly in a 0.31 m³ cage with 200 adult desert locusts which had been starved for 8–10 h. After 12 h of exposure to the hungry locusts, the damage suffered by each plant was assessed using a visual ranking index system. The same treated plants plus fresh controls were exposed in this way to starved locusts for 12 h after 1.5, 4, 7, 15, 21 and 25 days. The experiment was repeated three times using three replicates of each treatment and controls on each occasion. The locusts were still hungry at the end of each exposure and were ready to attack fresh control plants.

Table 1 Effects of Azadirachtin and Neem Preparations on *Schistocerca* attacking Young Bean Plants

Azadirachtin p.p.m.	Day		Alcoholic preparation p.p.m.	Day		Aqueous preparation p.p.m.	Day	
	1.5	15		1.5	15		1.5	15
10	0	1	100	0	1	1,000	0	1
1.0	0	2	10	0	3	100	0	3
0.5	0	3	2.5	0	4	80	0	4
0.2	0	4	1.0	1	5	40	1	5
0.1	1	5	0.5	1	5	20	1	5
0.05	1	5	0.2	1	5	10	2	5
0.01	1	5	0.1	1	5	1	4	5
Controls	5	5		4	5		5	5

Plant damage was assessed by a ranking index: 0, no feeding; 1, very slight nibbling, apical bud intact; 2, leaves partly eaten, some damage to apical bud; 3, apical buds and 1/3 of plant eaten; 4, a few lower buds remaining on stem only; 5, all the buds and most or all of the plant eaten. Treatments are expressed as parts per million of dry soil.

The results obtained shortly after treatment and after 15 days are given in Table 1. After 25 days the plants grown in the most heavily treated soil (10, 100, 1,000 p.p.m. of azadirachtin, alcoholic and aqueous preparations respectively) were still only slightly damaged by the hungry locusts.

Similar results have been obtained using older established plants of both tall and dwarf varieties, up to the fruiting stage. As soil composition is known to have an important bearing on the systemic uptake of chemicals by plants, experiments have been carried out with five different types of soils. The results indicate that high organic content and alkalinity in soils reduce the systemic anti-feeding activities of azadirachtin and the two crude neem preparations.

In other trials, bean seedlings grown from seeds soaked for 24 h in 0.01, 0.1 and 1% solutions of azadirachtin, alcohol extract and kernel water extract, respectively, were protected against damage by *Schistocerca* adults for one week after germination in cage feeding tests.

Plant nematodes of the genus *Pratylenchus* are also deterred by seedling treatments. When barley seedlings were dipped in a 1% aqueous suspension of crushed neem kernels for 2 h, then grown in a naturally infested soil for ten days, there was a decrease (> 50%) in the number of nematodes invading the developing root system. Further experiments are in progress to establish whether active compounds other than azadirachtin are present in neem extracts, using several species of test insect.

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² Fraenkel, G., *Entomol. Exp. Appl.*, **12**, 473 (1969).

³ Pradhan, S., Jotwani, M. G., and Rai, B. K., *Indian Fmg.*, **12**, 7 (1962).

⁴ Haskell, P. T., and Mordue, A. J., *Entomol. Exp. Appl.*, **12**, 591 (1969).

⁵ Butterworth, J. H., and Morgan, E. D., *Chem. Commun.*, **23** (1968).

HL-A Antigens on Human Trophoblast Cells

IN an outbred population, the placenta is essentially an allograft and many hypotheses have been put forward to explain why it is not rejected by the mother during pregnancy. One possibility is that placental tissue is devoid of transplantation antigens or these antigens are prevented from being expressed.

In mice, transplantation antigens are present on trophoblast cells, but this effect is masked by a coating of inert sialomucin material^{1,2}. There is only circumstantial evidence³, however, that an analogous situation pertains in humans. By the use of monolayer cultures of human trophoblast cells, we have been able to show in cytotoxicity *in vitro* tests that HL-A antigens are present.

Cultures of trophoblast and foetal skin cells were obtained as before⁴: cells were removed with 0.1% trypsin, and resuspended in Hanks solution to a concentration of 1×10^6 cells/ml.

Cytotoxic tests were performed on siliconed Clay-Adams ceramic ring slides using 0.025 ml. unit volumes. Cells were tested against: serum of the mother from whom the placenta was obtained; a multispecific anti-HL-A serum (Burke) which gives a strong cytotoxic reaction with the lymphocytes of more than 70% of Caucasian populations; a monospecific anti-HL-A2 serum (Wolfe).

Controls were set up by incubating the cells with: serum from a group AB rhesus positive nulliparous woman (Mar-

Table 1 Reaction of Trophoblast and Foetal Cells with Anti-HL-A Serum

Grade	Average % dead
—	0
(w)	5
w	15
(+)	30
+	50
(+ +)	75
+ +	100

chand) who has had no blood transfusions; Hanks only; Hanks and complement; the multispecific anti-HL-A serum without the addition of complement.

The mixtures were incubated at 37° C for 1 h in a moist container. Each test was then stained with 0.025 ml. of 0.4% trypan blue and read with a phase contrast microscope.

Both serum Burke and serum Wolfe were derived from group A rhesus positive individuals. After testing against a 'Selectogen' red cell panel, natural anti-B antibody was found in both sera but there was no evidence of antibody towards any of the following red cell antigens: rhesus C.D.E. $\bar{c}$.e.f.c.^W, Kell, Duffy, Kidd, Lewis, MNS, P, Lutheran, Vell, and Xg^a.

Trophoblast cells from four different placentae (T9, T13,

and it seems likely that this activity is directed against HL-A determinants. Incompatibility due to ABO groups can be definitely excluded in one case where both parents are group O. Furthermore, both serum Burke and serum Wolfe were found to possess natural anti-B only; no antibodies against other red cell antigens could be demonstrated. The monospecific anti-HL-A2 serum Wolfe was cytotoxic to one out of three trophoblasts tested, the frequency of the HL-A2 phenotype being about 49% in the Cambridge panel.

The finding of HL-A antigens on trophoblast cells *in vitro* does not nullify the concept that these determinants may be masked *in vivo*. There have been numerous reports on the presence of a covering layer around human trophoblast cells which may fulfil this function¹⁰⁻¹³.

In some cases, however, foeto-maternal immunization certainly occurs as indicated by the presence of anti-leucocyte antibodies in the serum of multiparous women^{14,15}. It seems likely that the trophoblast may at least partly be the source of the antigenic stimulation especially as these cells are widely deported in the maternal circulation during human pregnancy^{16,17}. There is a positive correlation between maternal sensitization and parity¹⁸. In our series, there was no demonstrable activity of maternal sera towards their respective trophoblast and foetal skin cells.

Table 2 Reactions of Trophoblast and Foetal Skin Cells with anti-HL-A Sera, Maternal Sera and Controls

	Multi-specific serum + complement	Multi-specific serum + Hanks	Anti-HL-A2 serum + complement	Control AB serum + complement	Maternal serum + complement	Hanks + complement	Hanks
Trophoblast (T9)	(+ +)	—	ND	W	W	—	—
Trophoblast (T13)	(+ +)	—	W	W	(W)	(W)	W
Trophoblast (T15)	(+ +)	—	W	(W)	W	W	(W)
Trophoblast (T16)	(+ +)	—	(+ +)	—	ND	(W)	(W)
Foetal skin (S9)	(+ +)	—	ND	W	(W)	—	—
Foetal skin (S13)	(+ +)	—	ND	—	(W)	—	—
Foetal skin (S15)	(+ +)	—	ND	(W)	W	(W)	—

ND, Not done.

T15, T16) were used. In one of these (T13), blood groups of both parents were ascertained to be group O Rhesus positive. The placenta in this case would therefore also be group O. This mother had had two previous pregnancies. The three other mothers were primigravidae. Corresponding cultures of foetal skin cells (S9, S13, S15) were also used.

The tests were scored according to the method described by Joysey⁵ as shown in Table 1.

Both trophoblast and foetal skin cells reacted strongly with the multispecific anti-HL-A serum Burke, the cytotoxic activity being complement dependent (Table 2). The monospecific anti-HL-A2 serum Wolfe was cytotoxic to one out of three trophoblasts tested. None of the maternal sera had any cytotoxic activity towards their respective trophoblast or foetal skin cells.

Currie and Bagshawe⁶ demonstrated that maternal as well as allogeneic lymphocytes had a cytotoxic effect on human trophoblast cells and concluded that trophoblast must have antigenic groupings foreign to the mother. Hulka *et al.*⁷ found that fluorescein-labelled serum globulin obtained from post-partum women would localize in placental tissue. These experiments provide evidence for the existence of antigens on human trophoblast cells, but do not indicate whether these are HL-A determinants.

Van Rood⁸ reported that serum containing anti-leucocyte antibodies was absorbed by placental tissue but Seigler and Metzgar⁹ were unable to confirm the presence of HL-A antigens on whole trophoblast.

The results of our experiment have shown that a serum containing strong multispecific anti-leucocyte antibody has cytotoxic activity towards human trophoblast cells *in vitro*,

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¹ Kirby, D. R. S., Billington, W. D., Bradbury, S., and Goldstein, D. J., *Nature*, **204**, 548 (1964).

² Currie, G. A., Van Doorninck, W., and Bagshawe, K. D., *Nature*, **219**, 191 (1968).

³ Billington, W. D., *Immunology and Development* (Spastics International Medical Publications, London, 1969).

⁴ Loke, Y. W., and Borland, R., *Nature*, **228**, 561 (1970).

⁵ Joysey, V. C., *Proc. Symp. Transpl. Antigens Tissue Typing* (1968).

⁶ Currie, G. A., and Bagshawe, K. D., *Advance in Transplantation* (Munksgaard, Copenhagen, 1967).

⁷ Hulka, J. F., Brinton, V., Schaaf, J., and Baney, C., *Nature*, **198**, 501 (1963).

⁸ Van Rood, J. J., *Leukocyte Grouping* (Drukkerij Pasmans, Den Haag, 1962).

⁹ Seigler, H. L., and Metzgar, R. S., *Transplantation*, **9**, 478 (1970).

¹⁰ Wynn, R. M., *Amer. J. Obstet. Gynecol.*, **97**, 832 (1967).

¹¹ Tighe, J. R., Garrod, P. R., and Curran, R. C., *J. Pathol. Bacteriol.*, **93**, 559 (1967).

¹² Boyde, J. D., Hamilton, W. J., and Boyde, C. A. R., *J. Anat.*, **102**, 553 (1968).

- ¹³ Bradbury, S., Billington, W. D., Kirby, D. R. S., and Williams, E. A., *Amer. J. Obstet. Gynecol.*, **104**, 416 (1969).
¹⁴ Payne, R., and Rolfs, M. R., *J. Clin. Invest.*, **37**, 1756 (1958).
¹⁵ Van Rood, J. J., Eernisse, J. G., and Van Leeuwen, A., *Nature*, **181**, 1735 (1968).
¹⁶ Douglas, G. W., Thomas, L., Carr, M., Cullen, N. M., and Morris, R., *Amer. J. Obstet. Gynecol.*, **78**, 960 (1959).
¹⁷ Attwood, H. D., and Park, W. W., *J. Obstet. Gynaecol. Brit. Cwlth*, **68**, 611 (1961).
¹⁸ Terasaki, P. I., Mickey, M. R., Yamazaki, J. N., and Vredevoe, D., *Transplantation*, **9**, 538 (1970).

Transplantation of Radiation-induced Canine Myelomonocytic Leukaemia

AN important variant of leukaemia in man is the myelomonocytic form¹, the exact nature of which is still unclear, for the only available model for studies of this disease is the mouse². We have developed a canine model which shows promise for studies of certain aspects of the pathogenesis of myelomonocytic leukaemia (MML) as related to changes that develop in a single animal. Because dogs live longer and are larger than mice, they are well suited to serial samplings of blood, bone marrow and other tissues, facilitating dynamic studies of changes in the haematopoietic system occurring with time.

Beagles continuously exposed to high ⁹⁰Sr concentrations developed a myeloproliferative syndrome (MPS)³. Several further cases of MPS were observed subsequently, including two of myelomonocytic leukaemia, and studies were undertaken to develop a canine model to aid studies of the aetiology, pathogenesis, diagnosis and possible control of the disease. This report concerns the transplantation of cells from one of the dogs with MML; similar studies utilizing cells from the other case produced comparable results.

The donor dog (D50F52), fed ⁹⁰Sr daily from birth, had accumulated about 5,000 rad of β -radiation to the bone marrow during her life. The diagnosis of MML (made when the dog was about 5 yr old) was based on haematological changes and confirmed by terminal pathological findings. There was a persistent significant increase in peripheral white blood cell numbers, especially granulocytes (including occasional blast forms) and monocytes. There was also an extreme increase in the percentage of granulocytes relative to other cell types in all samples of bone marrow examined (Table 1). Approximately 30% of the granulocytes in the terminal marrow samples were primitive, often atypical blast forms. Terminal lesions consisted of extensive invasion of haematopoietic organs (bone marrow, liver, spleen and lymph nodes), often with complete obliteration of the normal structure. In all the organs except the spleen, the tumour infiltrates appeared as fleshy green masses (chloroma). Most other organs and tissues contained focal accumulations of tumour cells.

Primary transplantation was accomplished with bone marrow cell preparations. Subsequent transplantations were done with cells from solid tumours or tumour ascites. The number of viable cells used in the inoculum varied from 1×10^7 to 2×10^8 cells ml⁻¹. The pregnant beagles used as recipients were not related to the donor dogs. Transplantation was effected by performing a laparotomy at 46–53 days of gestation and inoculating the foetuses intraperitoneally through the uterine wall⁴. Except in passage 5, at least one foetus in each litter served as a control and was inoculated with a radionuclide marker only, for identification⁴.

Animals were usually killed about a week after enlarged lymph nodes or solid tumours became evident and haematologic abnormalities were observed, which occurred 8–71 days after birth (Fig. 1).

Lesions observed in all five passages closely resembled those in the original donor dog, but were more pronounced. The population of neoplastic cells in the recipients consistently had more primitive cell types than the donor population. A

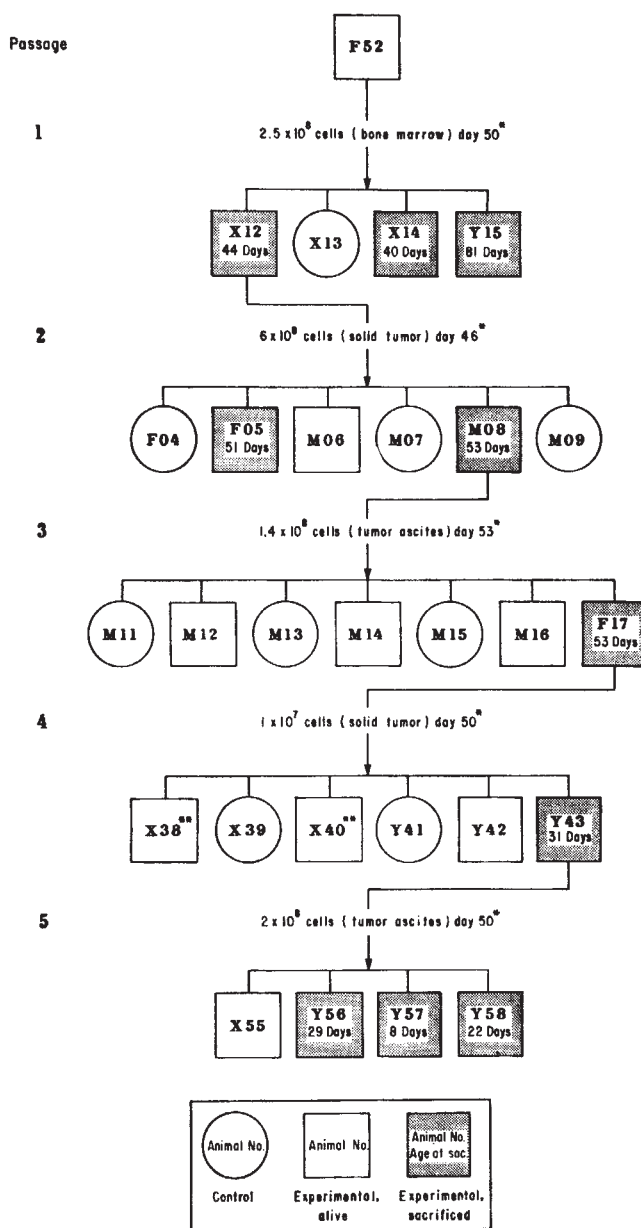


Fig. 1 Transplantation of myelomonocytic leukaemia.

*, Day of gestation inoculated; **, died at birth.

further prominent feature was the occurrence, in all recipients, of large retroperitoneal masses of chloromatous tumour tissue in the sublumbar region, comprising up to 10% of the host's body weight. Peripheral blood, serum lysozyme and bone marrow values for the donor and one passage 3 recipient which manifested a severe case of MML, are presented in Table 1. All control pups had normal haemograms, and no lesions were seen in the nine control pups that were killed.

Serum lysozyme concentrations, assayed by the method of Osserman and Lawlor⁵, were high in the primary donor and in all recipients that developed MML, whereas lysozyme was not detected in pups that did not manifest the disease (Table 1). Increased lysozyme concentrations, primarily in urine, are found in cases of human MML, which is considered to be of value in diagnosis⁵. Electron microscopic examination of tumour tissues has not revealed any virus particles. Further work is in progress to determine the possibility of a viral aetiology for the disease.

Chromosome analysis was performed on direct preparations of bone marrow, of peripheral and mesenteric lymph nodes

Table 1 Terminal Values for Peripheral Blood, Serum Lysozyme and Bone Marrow in Donor Dog and One Recipient with a Marked Case of Myelomonocytic Leukaemia

Parameter	Dog No.		Normal values (mean)*
	D50F52 (donor)	T14F17 (passage 3)	
Haematocrit (%)	32.1	26.4	30.0
Total leucocytes ($\times 10^3 \text{ mm}^{-3}$)	142.3	105.7	16.7
Leucocyte differential (in absolute numbers in thousands as percentage of total)			
Immature granulocytes†	5.7 (4)	30.7 (29)	0.6 (3.6)
Segmented neutrophils	82.5 (58)	24.3 (23)	7.8 (46.8)
Lymphocytes	19.9 (14)	14.8 (14)	6.0 (35.9)
Monocytes	17.1 (12)	4.2 (4)	1.8 (10.8)
Eosinophils	0 (0)	0 (0)	0.5 (2.9)
Unclassified cells	17.1 (12)	31.7‡ (30)	
Serum lysozyme ($\mu\text{g ml}^{-1}$)	250	130	0
Marrow granulocytic series (percentage of total granulocytes)§			
Myeloblasts	32	30	0.7
Promyelocytes	9	14	1.2
Myelocytes	30	19	6.8
Metamyelocytes	15	13	23.1
Bands	9	21	32.6
Segmented	3	2	35.6
Mitotic figures	2	1	0
Myeloid : erythroid ratio (M/E)	57	56	1.2

* Peripheral blood: mean values of fifteen normal 38 to 52 day old pups. Marrow: mean values of multiple samples of rib marrow from twelve young adult beagles.

† Promyelocytes, myelocytes, metamyelocytes, and bands.

‡ Data are presented as percentage of granulocytes rather than of total cells because few cells were seen other than granulocytes, as evident from the M/E ratio.

§ Unclassified cells consist of atypical blast cells and abnormal cells with the morphological characteristics of both granulocytic and monocytic elements.

and of solid and ascitic tumour material. Cytogenetic evaluation of the recipient puppies, by analysis of the males' sex chromosomes, showed conclusively that the tumour tissues consisted of the original female donor cells. Most of the cells examined from all the recipient puppies contained a very small, abnormal, acrocentric autosome which may be a disease-specific marker comparable with the Philadelphia chromosome that is characteristic of chronic granulocytic leukaemia in man.

To sum up, we have demonstrated, by the transplantation of malignant cells, the feasibility of using the dog as a model for the study of myelogenous leukaemia.

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¹ Linman, J. W., *J. Chronic Dis.*, **22**, 713 (1970).

² Warner, N. L., Moore, M. A. S., and Metcalf, D., *J. Nat. Cancer Inst.*, **43**, 963 (1969).

³ Dungworth, D. L., Goldman, M., Switzer, J. W., and McKelvie, D. H., *Blood*, **34**, 610 (1969).

⁴ Stone, J. M., and Shifrine, M., *J. Immunol.*, **104**, 1562 (1970).

⁵ Osserman, E. F., and Lawlor, D. P., *J. Exp. Med.*, **124**, 921 (1966).

Persistent Corpora Lutea of Mice in a Cold Environment

If laboratory mice, *Mus musculus*, are bred in permanently mated pairs in an environment kept at -3°C , their litters are usually smaller at birth than those of controls at 21°C . Cold adaptation is also accompanied by differences in the relative weights of many organs and tissues²⁻⁴. In particular, the gonads, at least of unmated mice, tend to be lighter in a cold environment.

Smaller litters in a cold environment could be due to a lower ovulation rate or to higher losses of embryos before or after implantation. During an investigation of this and allied questions, we have made an apparently novel observation on the ovaries of cold-adapted mice. The laboratory mice were of several types, mated in separate pairs at the age of 5 weeks and allowed to rear their first litters. The males were removed shortly before the birth of the second litters, which were killed within 24 h of parturition. The males were then replaced, and the females watched for the appearance of a vaginal plug. Fifteen days after a plug was recorded, that is, on the sixteenth day of gestation, each female was killed and dissected. The ovaries were quickly removed, cleaned, weighed to the nearest 0.1 mg, fixed, serially sectioned and stained; the corpora lutea were then counted. The number of foetuses and abnormal implantations was also recorded. Some wild house mice were studied⁵: they were similarly treated, except that the males were not removed and the females were killed when visibly in late pregnancy.

The first anomalous finding was that the ovaries of the cold-adapted, pregnant mice were heavier than those of the controls. Table 1 illustrates this from mice of strain A2G/Tb, for which we also have weights of the ovaries of virgin mice at both temperatures; the ovaries of the virgins, unlike those of the pregnant females, were lighter at -3°C . The discrepancy in ovarian weights in pregnancy was due to a difference in the number of corpora lutea in the two temperatures. Table 2

Table 1 Mean Weights (mg) $\pm$ s.e. of Ovaries of A2G/Tb Mice

	21° C		-3° C†		P < ‡
	N		N		
Virgin*	16	21.9 $\pm$ 1.2	13	16.4 $\pm$ 2.2	0.01
Pregnant	25	19.1 $\pm$ 0.9	21	29.4 $\pm$ 1.3	0.001

* From Barnett and Widdowson².

† First generation reared in cold.

‡ Student's *t* test.

Table 2 Corpora Lutea and Foetuses of Mixed Stock

	21° C	21 $\rightarrow$ -3° C	-3° C*	-3° C†
No. of mice	32	35	25	28
Corpora lutea	19.1 $\pm$ 0.9	34.2 $\pm$ 1.5	34.8 $\pm$ 1.3	27.2 $\pm$ 1.5
Foetuses	10.6 $\pm$ 0.6	9.8 $\pm$ 0.5	12.4 $\pm$ 0.6	10.3 $\pm$ 0.7

Figures are means $\pm$ s.e.

* Generation 1.

† Generations 27 to 31.

Table 3 Corpora Lutea and Foetuses of Inbred and F₁ Mice

	21° C	21→-3° C	-3° C
C57BL/Tb			
No. of mice	25	23	—
Corpora lutea	12.2±0.8	18.4±0.9	—
Foetuses	8.4±0.5	8.0±0.8	—
A2G/Tb			
No. of mice	25	22	21*
Corpora lutea	16.2±0.7	29.6±1.0	29.4±1.8
Foetuses	9.0±0.6	8.6±0.6	9.7±0.7
F₁			
No. of mice	23	28	—
Corpora lutea	16.1±0.8	23.5±1.0	—
Foetuses	13.1±0.4	12.6±0.4	—
Wild			
No. of mice	10	—	12†
Corpora lutea	8.4±0.4	—	12.8±1.2
Foetuses	6.4±0.4	—	9.2±1.1

Figures are means ± s.e.

* First generation reared in the cold.

† Ninth generation reared in the cold.

gives figures for three classes of cold-adapted mice of a mixed, outbred stock. Mice which had been transferred to the cold environment as young adults before mating (21→-3° C), and those of the first generation reared at -3° C, had about 80% more corpora lutea than the controls. Mice of the same origin after many generations in the cold environment had about 42% more corpora lutea. Table 2 also shows that the number of viable foetuses was not correspondingly higher in the cold.

females at 21° C was 5.6±0.5; the corresponding figure for six females at -3° C was 5.7±0.7. Hence the excess of corpora lutea at -3° C does not represent a raised ovulation rate in these mice. A methodological conclusion follows: the number of corpora lutea, at least in a mouse ovary, should not be assumed always to correspond to the effective ovulation rate. This applies especially in unusual environments.

In the eleven classes of laboratory mice the mean number of abnormal conceptions ranged from 0.87 to 2.69. The wild mice had almost none. Evidently, therefore, losses after implantation were few. There was also little or no effect of cold on the litter sizes of the laboratory mice (that is, number of normal foetuses at 16 days). This differs from previous findings¹ because the mice of the present study were never rearing a litter of sucklings during gestation, as were some of those studied in earlier work.

In experimental work on the cold-adaptation of mammals, exposure to cold is rarely longer than a few weeks, and effects on reproduction have usually been neglected. Attention has been concentrated on the changes which take place while an isolated small laboratory mammal is adjusting to a sudden lowering of environmental temperature³. In contrast, our mice at -3° C were presumably in metabolic and hormonal equilibrium. Nevertheless, this probably entailed pituitary and adrenal cortical activity above that at 21° C. Adrenal weights are given in Table 4; except the F₁ mice, which had heavy adrenals even in the warm environment, all classes at -3° C had heavier adrenals than at 21° C.

The large numbers of corpora lutea in the cold were probably due to persistence of the corpora lutea from a previous ovulation, resulting from the altered endocrine activity. This requires further study. So does the larger litter size of wild mice at -3° C. If these phenomena regularly accompany

Table 4 Adrenal Weights

	Mixed stock		C57BL/Tb		A2G/Tb		F ₁		Wild	
	N		N		N		N		N	
21° C	11	4.7±0.3	22	4.7±0.3	23	4.7±0.3	22	5.5±0.2	9	5.0±0.6
21→-3° C	32	6.2±0.4†	19	7.0±0.5‡	20	5.5±0.2*	27	5.6±0.3	—	—
-3° C	20	5.8±0.5	—	—	19	5.9±0.4*	—	—	12	6.8±0.6*

Figures are means ± s.e. * $P < 0.05$ (Student's t test). † $P < 0.01$ (Student's t test). ‡ $P < 0.001$ (Student's t test).

The effect of cold on the ovary was not a peculiarity of one type of mouse. Table 3 gives the figures for corpora lutea of mice of two inbred strains, A2G/Tb and C57BL/Tb, the F₁ generation produced by crossing them, and of wild house mice. All showed a similar effect of cold. The findings from the mixed stock (Table 2) and from strain A2G/Tb show that the effect on the ovary of transfer to -3° C at mating was the same as that of being reared (first generation) in the cold. All differences between temperatures in number of corpora lutea are statistically significant ($P < 0.01$; Student's t). The wild mice, unlike the laboratory mice, also had larger litters in the cold environment ($P < 0.05$).

The number of corpora lutea is usually regarded as a reliable index of the number of ova shed at the most recent ovulation. If it were so for our laboratory mice, we should have to assume exceptionally high ovulation rates in the cold environment, and corresponding losses before implantation. To test this, more pairs of the mixed stock were transferred to -3° C; pairs from the same litters were also mated at 21° C. When a vaginal plug indicated the beginning of the third pregnancy, the female was killed. The ovaries and fallopian tubes were removed, fixed and stained, and the eggs shed at that ovulation were counted. The mean number of ova per tube from nine

the cold-adaptation of other mammals, the question arises whether they occur also in other adverse conditions, such as exceptional crowding. It would be interesting to know more about the corpora lutea of species which, in their natural environment, continue to reproduce in varying conditions of climate, feeding and other environmental features.

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¹ Barnett, S. A., *Quart. J. Exp. Physiol.*, **49**, 290 (1964).

² Barnett, S. A., and Widdowson, E. M., *Proc. Roy. Soc., B*, **162**, 502 (1965).

³ Barnett, S. A., and Mount, L. E., in *Thermobiology* (edit. by Rose, A. S.) (Academic Press, London, 1967).

⁴ Barnett, S. A., and Widdowson, E. M., *J. Reprod. Fert.* (in the press).

⁵ Barnett, S. A., Smart, J. L., and Stoddart, R. C., *J. Zool.*, **163**, 443 (1971).

Molecular Pathology of Human Haemoglobin: Stereochemical Interpretation of Abnormal Oxygen Affinities

WHEN the atomic model of oxyhaemoglobin had just been completed, we showed that the haemoglobin molecule is insensitive to replacements of most amino-acid residues on its surface but extremely sensitive to quite small alterations of internal non-polar contacts. And replacements near the haems and at the contacts between α and β subunits affect the respiratory function¹.

Many amino-acid substitutions in abnormal haemoglobins produce clinical symptoms by altering the oxygen affinity. Now that the atomic structures of both deoxy and oxyhaemoglobin are known^{2,3} and a cooperative mechanism has been proposed⁴, we can try to interpret these abnormal oxygen affinities in stereochemical terms. In the first instance, the oxygen affinity depends on the conformation of the globin

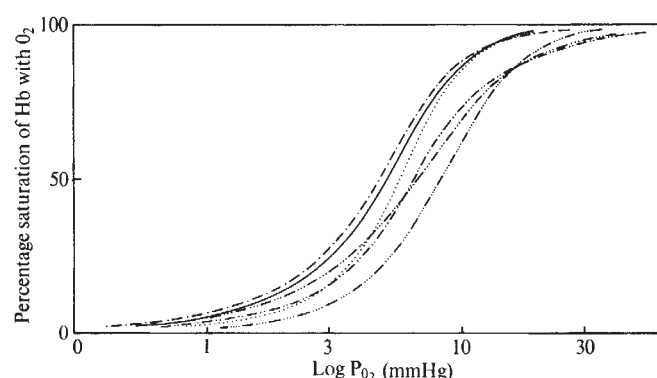


Fig. 1 Oxygen equilibrium curves of haemolysates containing unstable abnormal haemoglobins.

	Concentrations of abnormal haemoglobins	Methaemoglobin concentration	
		before	after
· From normal person		1.5%	4.0%
· - A+Borås	10%	5.5%	7.5%
· - A+Shepherd's Bush	16%	8.0%	12.0%
· - A+Hammersmith	30%	6.5%	12.0%
· - A+Bucuresti	15%	11.5%	13.0%
· - Lepore Boston +	27%	2.5%	4.5%
	(Lepore)		
Peterborough	70%		
	(Peterborough)		

Except for haemoglobins A, Peterborough and Lepore Boston, haemolysates were prepared without the use of organic solvents, with water and dilution appropriate buffers. Haemoglobin Peterborough (Fig. 2) was separated from Lepore and its purity checked by starch gel electrophoresis. Haemoglobin Borås was also separated by starch block electrophoresis; it showed a high oxygen affinity and a Bohr effect, but quantitative data were not obtained. For haemoglobin Shepherd's Bush see Table 2. Oxygen equilibrium curves were determined by the method of Imai *et al.*⁷ which involved the use of monochromatic light at 480 nm with haemoglobin at a concentration of 6×10^{-5} M/haem in 0.1 M K_2HPO_4 , KH_2PO_4 and 0.5 mM EDTA (pH 7.43 $\pm$ 0.02) at 20° C. The concentration of methaemoglobin was checked spectrophotometrically before and after the measurement, using the optical density ratio at 508 nm and 576 nm. The spectra of abnormal methaemoglobins were assumed to be the same as the spectrum of the normal form, and the ratio of the absorption coefficients was assumed to be 3.20 when the methaemoglobin concentration was zero. The concentrations of the abnormal haemoglobins were calculated from optical densities of protein (280 nm) and haem (540 nm) of the cyanomet form in the supernatant after incubating the haemolysate for one hour in 0.05 M Tris-HCl buffer of pH 7.4. The concentrations of haemoglobins Lepore Boston and Peterborough were determined by chromatographic separation. Since carbon tetrachloride was used for preparing the haemolysates for the estimations of fractional concentration, the concentration of the abnormal haemoglobins in the fresh blood may be higher than in the haemolysates.

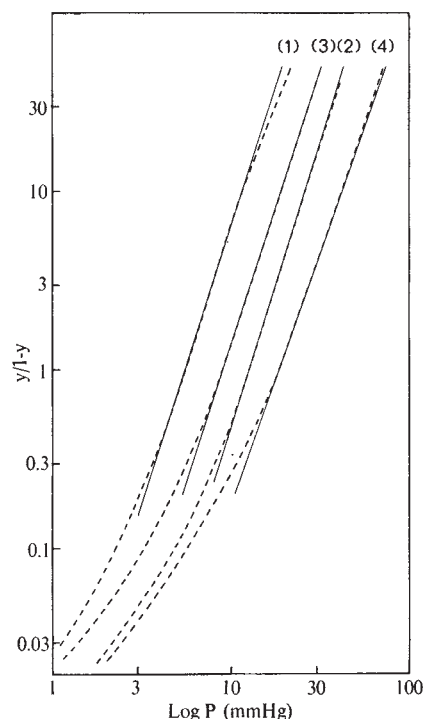


Fig. 2 Hill's constants of haemoglobins A (haemolysate) and Peterborough.

	pH	Hill's constant	Methaemoglobin concentration	
			before	after
(1) Haemoglobin A	7.41	3.1	1.0%	2.5%
(2) Haemoglobin A	6.56	3.2	1.0%	2.5%
(3) Haemoglobin Peterborough	7.42	3.0	2.0%	3.5%
(4) Haemoglobin Peterborough	6.56	2.8	4.0%	8.0%

y, Fractional saturation of haemoglobin with oxygen; P, oxygen partial pressure. Conditions as for Fig. 1. The Bohr effect of haemoglobin Peterborough is seen to be normal.

pocket surrounding the haem group and on residues known to be involved in the Bohr effect or the binding of 2,3-diphosphoglycerate. But in other cases of abnormal oxygen affinity the substituted residues are far removed from any of the binding sites for either oxygen, hydrogen ions or 2,3-diphosphoglycerate. We have found that several of these substitutions alter the oxygen affinity by their effect on the allosteric equilibrium between either the two alternative tertiary structures of the individual subunits or the two alternative quaternary structures of the haemoglobin tetramer.

We have considered some cases of abnormal oxygen affinity recorded in the literature, and others recently detected here, which are shown in Figs. 1 and 2. Table 1 lists four substitutions which alter the conformation of the haem pocket: haemoglobins Zürich and Bristol throw light on the part played by the distal histidine E7 which is present in all mammalian haemoglobins (though absent in *Chironomus*⁵ and *Aplysia*⁶). Model building suggests that oxygen may not be able to get into or out of the haem pocket unless that histidine swings out of the way; in haemoglobin Zürich it is replaced by arginine which cannot be accommodated in the haem pocket and leaves it open. This gives rise to a very high oxygen affinity. In haemoglobin Bristol, on the other hand, the histidine must be held firmly in position by a salt bridge connecting it to an internal aspartate (E11); this lowers the oxygen affinity, though it is not clear how the oxygen gets in and out at all in these conditions. The substitution of phenylalanine CD1 by serine in haemoglobin Hammersmith and by leucine in Bucuresti may lower the oxygen affinity because the benzene ring of the phenylalanine in haemoglobin A acts as a spacer that stabilizes the haem group

Table 1 Substitution of Residues Directly Affecting the Oxygen Binding Site

Refer- ences	Designation	Residue No.	Position	Replacement from to	Variability	Clinical symptoms	Oxygen affinity (Hill's constant; Bohr effect)	Effect of replacement on equilibrium between deoxy and oxy forms
8, 9	Hammersmith	β 42	CD1	Phe Ser	I	Severe, haemolytic anaemia, splenomegaly. Heinz bodies after splenectomy	Low	The haem group changes its tilt from a more upright position in deoxy to a more inclined one in oxyhaemoglobin. Phe CD1 acts as a spacer that keeps it in the more inclined position; its removal would facilitate the transition to the more upright one in the deoxy form
37	Bucuresti	β 42	CD1	Phe Leu	I	Mild haemolytic anaemia. Spleen palpable	Low	As above
10-12	Zürich	β 63	E7	His Arg	I	Haemolytic inclusion body anaemia on treatment with sulphonamides	Very high (1.8; nearly normal)	The arginine cannot be accommodated in the haem pocket, leaving a large cavity at the ligand site of the iron atom. The haem pocket is wide open
13, 14	Bristol	β 67	E11	Val Asp	I	Haemolytic anaemia with splenomegaly, methaemoglobin formation	Low	Asp at E11 forms a salt bridge with His E7 which would keep the haem pocket tightly closed. Also the carboxyl group would sterically interfere with the bound oxygen
15, 16	Borås	β 88	F4	Leu Arg	I	Mild haemolytic anaemia with spleno- megaly. Tendency to methaemoglobin formation	High	The replacement would leave a gap in the haem pocket which apparently makes the haem group more susceptible to autoxidation. This may be the cause of the high oxygen affinity

The positions of all these residues are shown in Fig. 2 of ref. 1. In this and the following tables, Hill's constant and Bohr effect, if determined, are indicated in brackets after the oxygen affinity. References refer to structure, oxygen affinity, and clinical symptoms, in that order. Variability refers to mammalian species only.

Table 2 Substitution of Residues Affecting the Balance Between the Two Alternative Tertiary Structures

Refer- ences	Designation	Residue No.	Residue Position	Replacement from	to	Variability	Clinical symptoms	Oxygen affinity (Hill's constant; Bohr effect)	Effect of replacement on equilibrium between deoxy and oxy forms
17-19	E	β 26	B8	Glu	Lys	I	None in heterozygotes. Mild haemolytic anaemia in homo- zygotes under stress	Low (normal; normal)	Glu B8 β is bound to His G19 β in both oxy and deoxy. Its replacement by Lys would introduce a positively charged side chain in oxy where Arg B12 β , His G18 and 19 β are already closely clustered. In deoxy, on the other hand, the lysyl side chain could be much further away from this cluster. Therefore, the replacement would stabilize the oxy, but not the deoxy, structure
20	Shepherd's Bush	β 74	E18	Gly	Asp	V	Mild haemolytic anaemia with splenomegaly	High, P_{50} 3.7 at pH 7.4 with P_{50} 6.3 for HbA control; (reduced, 2.5 at pH 7.4 with 3.4 for HbA control; normal)	In oxy the side chain of the Asp is easily accommodated, but in deoxy it comes too close to Phe F1, which would make the tertiary deoxy structure unstable
21, 22	Seattle	β 76	E20	Ala	Glu	V	Mild anaemia	Very low (2.1; nearly normal)	Unexplained
23, 24	Agenogi	β 90	F6	Glu	Lys	I	None	Low (normal; normal)	Lys F6 β could form a salt bridge with the C-terminal carboxyl of the same β -chain in oxyhaemoglobin. This would push tyrosine HC2 into its pocket between helices F and H, which is its deoxy position, and thus lower the oxygen affinity of the β -chains
38	Peterborough	β 111	G13	Val	Phe	V	Mild anaemia	Low (normal; normal)	In the deoxy form Phe G13 can be accom- modated in the $\alpha_1\beta_1$ contact by dis- placing the side chain or Gln H5 β without further disturbance of the struc- ture. In the oxy form, this is not possible. If oriented towards the $\alpha_1\beta_1$ contact, the side chain of Phe G13 would severely disturb it. If oriented within the β sub- unit it would make a short contact with Val H12 and produce dislocations. Hence, the replacement would destabi- lize the oxy, but not the deoxy, structure

The positions of the residue substituted in haemoglobins E and Agenogi are illustrated in Figs. 3 and 4 of ref. 1.

Table 3 Substitution of Residues Affecting the Balance Between the Two Alternative Quaternary Structures

Refer- ences	Designation	Residue No.	Position	Replacement from to	Variability	Clinical symptoms	Oxygen affinity (Hill's constant; Bohr effect)	Effect of replacement on equilibrium between deoxy and oxy forms
25,39	Hirose	$\beta 37$	C3	Trp Ser	I	None	Very high (1.5; quarter)	Trp C3 β_2 forms a vital part of the $\alpha_1\beta_2$ contact in both forms of haemoglobin. It is in contact with Tyr HC2 α_1 in deoxy, and occupies a position such that it would oppose the expulsion of that tyrosine from its pocket between helices F and H which occurs on oxygenation. Removal of Trp C3 β would therefore facilitate the transition to the quaternary oxy structure
26 *	Malmö	$\beta 97$	FG4	His Gln	I	Erythrocytosis	Very high	His FG4 lies at the $\alpha_1\beta_2$ contact but it is not clear why its replacement by Gln should change the oxygen affinity
27, 28	Yakima	$\beta 99$	G1	Asp His	I	Erythrocytosis	Very high (1.0; normal)	Asp G1 β_2 may be hydrogen bonded to NH of Glu G3 β_2 in oxy. In deoxy it is hydrogen bonded to the phenolic OH of Tyr C7 α_1 . The mutation breaks this important bond in the $\alpha_1\beta_2$ contact of the deoxy form and destabilizes the quaternary structure
29	Kempsey	$\beta 99$	G1	Asp Asn	I	Erythrocytosis	Very high	As above
30, 31	Kansas	$\beta 103$	G4	Asn Thr	I	Cyanosis	Very low (1.3; present)	Asn G4 β_2 forms a hydrogen bond with Asp G1 α_1 in oxy. The mutation breaks this important bond in the $\alpha_1\beta_2$ contact of the oxy form and destabilizes the quaternary oxy structure
32	Yoshizuka	$\beta 108$	G10	Asn Asp	I	Mild anaemia	Low (normal; reduced)	Asn G10 β_1 is in contact with His G10 α_1 , which lies in a buried position in the $\alpha_1\beta_1$ contact. The replacement of Asn by Asp may lead to the ionization of the histidine, but it is not clear how the degree of ionization would differ in the two alternative quaternary structures

* And personal communication from G. Berglund and T. Leonhardt.

The positions of the residues substituted in haemoglobins Hirose, Malmö, Yakima, Kempsey and Kansas are illustrated in Fig. 8 of ref. 38.

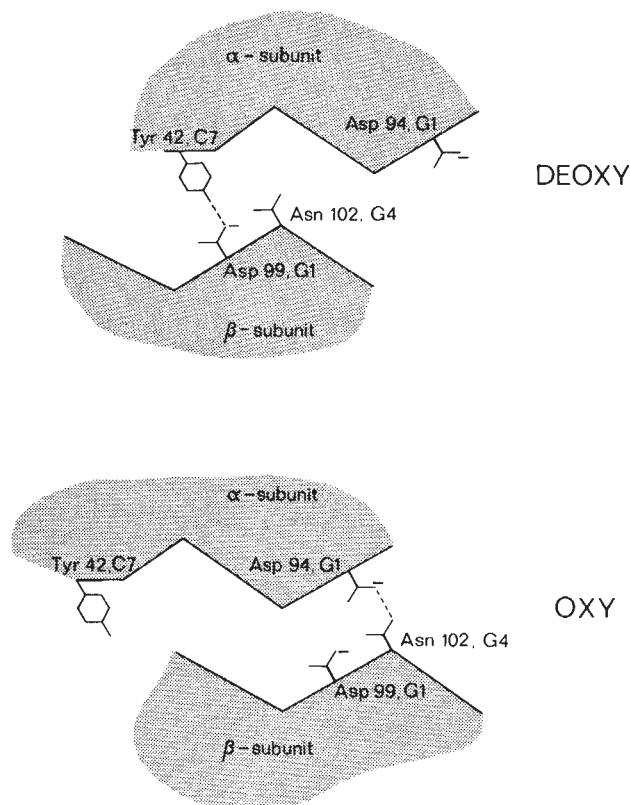


Fig. 3 Change in $\alpha_1\beta_2$ contact on oxygenation. The contact area clicks from one dovetailed position to another, involving a switch of hydrogen bonding as shown. Most of the other contacts are non-polar.

in the more inclined position which it takes up in the tertiary oxy structure. The removal of that ring in the two abnormal haemoglobins may make it easier for the haem group to turn to its more upright position in the deoxy structure.

Among the substitutions affecting the balance between the two alternative tertiary structures listed in Table 2, those of haemoglobins Shepherd's Bush and Peterborough seem to alter the relative free energies of the β subunits in the oxy and deoxy states by purely sterical effects. In Shepherd's Bush the substituted aspartic acid residue is a misfit only in the tertiary deoxy structure, which raises the oxygen affinity, while in Peterborough the substituted phenylalanine is a misfit only in the tertiary oxy structure, which lowers the oxygen affinity. In haemoglobin E the effect seems to be electrostatic, the oxygen affinity being lowered by a cluster of positively charged side chains that destabilizes the oxy structure. The substitution of lysine for glutamic acid in position F6 β in haemoglobin Agenogi is interesting because the lysine seems to interact with the C-terminal residues of the β -chain which regulate its oxygen affinity. In deoxyhaemoglobin, tyrosine HC2 β is tightly bound in a pocket between helices F and H, but on oxygenation that pocket narrows and the tyrosine is expelled⁴. Any forces which push the tyrosine back into its pocket, such as low pH, would also lower the oxygen affinity. Model building shows that a lysine in position F6 could force the tyrosine into its pocket by combining with the C-terminal carboxyl of histidine HC3 β . The alanine residue in position E20 is external; its substitution by glutamic acid in haemoglobin Seattle should have no effect on the oxygen affinity. Indeed, an acid group in this position probably occurs in several mammalian species. This haemoglobin may need further study.

The substitutions listed in Table 3 seem to alter the balance of interactions between the subunits. Tyrosine HC2 α_1 , like the corresponding tyrosine in the β -chain, is wedged into a pocket between helices F and H in the deoxy form and gets

expelled on oxygenation. This expulsion is opposed by the indol ring of tryptophan C3 β_2 . The two residues lie in the $\alpha_1\beta_2$ contact. Replacement of the tryptophan by serine in haemoglobin Hirose would ease the expulsion of the tyrosine and thereby raise the oxygen affinity. It would also open the α_1 and β_2 contact to water and thereby precipitate dissociation into dimers. Kansas, Yakima and Kempsey offer the most striking examples of mutations altering the allosteric equilibrium between the two alternative quaternary structures. They each affect the $\alpha_1\beta_2$ contact in the region between C α and FG β where the two subunits slide past each other by several Ångströms in the course of their reaction with oxygen. In each of the two forms the contact is made up of many van der Waals interactions plus one hydrogen bond (Fig. 3 and Fig. 1 of ref. 3). In deoxyhaemoglobin A that single hydrogen bond is between aspartate G1 β_2 and tyrosine C7 α_1 ; in oxyhaemoglobin A it is replaced by another between asparagine G4 β_2 and aspartate G1 α_1 . In Yakima and Kempsey, replacement of aspartate G1 β breaks the hydrogen bond that stabilizes the deoxy form, resulting in high oxygen affinity. In Kansas replacement of asparagine G4 β by threonine breaks the hydrogen bond that stabilizes the oxy form, resulting in low oxygen affinity (though there may be other factors; Greer found dislocations in the β subunits which may also affect their oxygen affinity³³).

A diminished Bohr effect has been reported for haemoglobin Yoshizuka. The replaced asparagine residue lies in the $\alpha_1\beta_2$ contact where histidine G10 α_1 is normally in contact with the amides of asparagine G10 β_1 and glutamine H9 β . Replacement of the asparagine by aspartic acid would tend to raise the pK of the neighbouring histidine, and if the rise were greater in oxyhaemoglobin than in deoxyhaemoglobin this would oppose the normal Bohr effect. But the atomic models do not suggest any reason why the degree of ionization of histidine G10 α in the two forms should differ. The very high oxygen affinity of haemoglobin Malmö is also puzzling. Histidine FG4 β is one of the invariant residues at the $\alpha_1\beta_2$ contact, but its part in the allosteric mechanism is still unclear. Similarly, haemoglobins Chesapeake and Capetown in which arginine FG4 α is replaced by leucine and glutamine respectively, show high oxygen affinity and low haem-haem interaction which are at present unexplained³⁴. Haemoglobin M Iwate has a very low oxygen affinity because it is permanently frozen in the quaternary deoxy structure³⁶. Haemoglobins M Milwaukee and Boston also have low oxygen affinities; they are still under X-ray study.

These results show that the equilibrium between the oxy and deoxy forms of haemoglobin can be altered in many ways. One of the two forms may be destabilized because the mutation introduces a bigger side chain which is a misfit in one form but not in the other, or because the mutation leads to a concentration of groups of equal charge which repel each other in one but not the other of the two forms or because it leads to the loss of a hydrogen bond stabilizing one or the other of the two quaternary structures. The equilibrium between the two allosteric forms of the haemoglobin molecule is shown to be very sensitively balanced so that the loss or gain of a single pair of hydrogen bonds has a drastic effect on the oxygen dissociation curve. It is encouraging that even fine modulations of physiological properties of some proteins can now be understood, at least qualitatively, on the basis of atomic models derived from X-ray analysis.

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- ¹ Perutz, M. F., and Lehmann, H., *Nature*, **219**, 902 (1968).
- ² Muirhead, H., and Greer, J., *Nature*, **228**, 516 (1970).
- ³ Bolton, W., and Perutz, M. F., *Nature*, **228**, 551 (1970).
- ⁴ Perutz, M. F., *Nature*, **228**, 726 (1970).
- ⁵ Buse, G., Braig, S., and Braunitzer, G., *Hoppe Seyl. Z.*, **349**, (1969).
- ⁶ Rossi Fanelli, A., Antonini, E., and Povoledo, D., *Symposium on Protein Structure* (edit. by Neuberger, A.), 144 (Methuen, London, 1958).
- ⁷ Imai, K., Morimoto, H., Kotani, M., Watari, H., Hirata, W., and Kuroda, M., *Biochim. Biophys. Acta*, **200**, 189 (1970).
- ⁸ Dacie, J. V., Shinton, N. K., Gaffney, P. J., Carrell, R. W., and Lehmann, H., *Nature*, **216**, 663 (1967).
- ⁹ Grimes, A. J., Meisler, A., and Dacie, J. V., *Brit. J. Haematol.*, **10**, 281 (1964).
- ¹⁰ Muller, C. J., and Kingma, S., *Biochim. Biophys. Acta*, **50**, 595 (1961).
- ¹¹ Winterhalter, K. H., Anderson, N. M., Amiconi, G., Antonini, E., and Brunori, M., *Europ. J. Biochem.*, **11**, 435 (1969).
- ¹² Hitzig, W. H., Frick, P. C., Betke, K., and Huisman, T. H. J., *Helv. Paediat. Acta*, **15**, 499 (1960).
- ¹³ Steadman, J. H., Yates, A., and Huehns, E. R., *Brit. J. Haematol.*, **18**, 435 (1970).
- ¹⁴ Cathie, I. A. B., *Great Ormond Street J.*, **2**, 43 (1952).
- ¹⁵ Hollender, A., Lorkin, P. A., Lehmann, H., and Svensson, B., *Nature*, **222**, 953 (1969).
- ¹⁶ Svensson, B., and Strand, L., *Scand. J. Haematol.*, **4**, 241 (1967).
- ¹⁷ Hunt, J. A., and Ingram, V. M., *Biochim. Biophys. Acta*, **49**, 520 (1961).
- ¹⁸ Thompson, R. B., Warrington, R. L., and Bell, W. N., *Amer. J. Physiol.*, **268**, 198 (1965).
- ¹⁹ Lehmann, H., Story, P., and Thein, H., *Brit. Med. J.*, **1**, 544 (1956).
- ²⁰ White, J. M., Brain, M. C., Lorkin, P. A., Lehmann, H., and Smith, M., *Nature*, **225**, 939 (1970).
- ²¹ Huehns, E. R., Hecht, F., Yoshida, A., Stamatoyanopoulos, G., Hartman, J., and Motulsky, A. G., *Blood*, **36**, 209 (1970).
- ²² Stamatoyanopoulos, G., Parer, J. T., and Finch, C. A., *New England J. Med.*, **281**, 915 (1969).
- ²³ Miyaji, T., Suzuki, H., Ohba, Y., and Shibata, S., *Clin. Chim. Acta*, **14**, 624 (1966).
- ²⁴ Imai, K., Morimoto, H., Kotani, M., Shibata, S., Miyaji, T., and Matsumoto, K., *Biochim. Biophys. Acta*, **200**, 197 (1970).
- ²⁵ Yanase, T., Hanada, M., Seita, M., Ohta, Y., Imamura, T., Fujimura, T., Kawasaki, K., and Yamaoka, K., *Jap. J. Human Genet.*, **13**, 40 (1968).
- ²⁶ Lorkin, P. A., Lehmann, H., Fairbanks, V., Berglund, G., and Leonhardt, T., *Biochem. J.*, **119**, 68P (1970).
- ²⁷ Jones, R. T., Osgood, E. E., Brimhall, B., and Koler, R. D., *J. Clin. Invest.*, **46**, 1840 (1967).
- ²⁸ Novy, M. J., Edwards, M. J., and Metcalfe, J., *J. Clin. Invest.*, **46**, 1848 (1967).
- ²⁹ Reed, C. S., Hampson, R., Gordon, S., Jones, R. T., Novy, M. J., Brimhall, B., Edwards, M. J., and Koler, R. D., *Blood*, **31**, 623 (1968).
- ³⁰ Bonaventura, J., and Riggs, A., *J. Biol. Chem.*, **243**, 980 (1968).
- ³¹ Reissman, K. R., Ruth, W. E., and Nomura, T., *J. Clin. Invest.*, **40**, 1826 (1961).
- ³² Imamura, T., Fujita, S., Ohta, Y., Hanada, M., and Yanase, T., *J. Clin. Invest.*, **48**, 2341 (1969).
- ³³ Greer, J., *J. Mol. Biol.*, **59**, 99 (1971).
- ³⁴ Greer, J., thesis, Univ. Cambridge (1970).
- ³⁵ Perutz, M. F., Muirhead, H., Cox, J. M., and Goaman, L. C. G., *Nature*, **219**, 131 (1968).
- ³⁶ Greer, J., *J. Mol. Biol.*, **59**, 107 (1971).
- ³⁷ Bratu, V., Lorkin, P. A., Lehmann, H., and Predescu, C., *Biochim. Biophys. Acta* (in the press).
- ³⁸ King, M. A. R., Wiltshire, B. G., and Lehmann, H., *Brit. J. Pharmacol.* (in the press).
- ³⁹ Yamaoka, K., *Blood* (in the press).

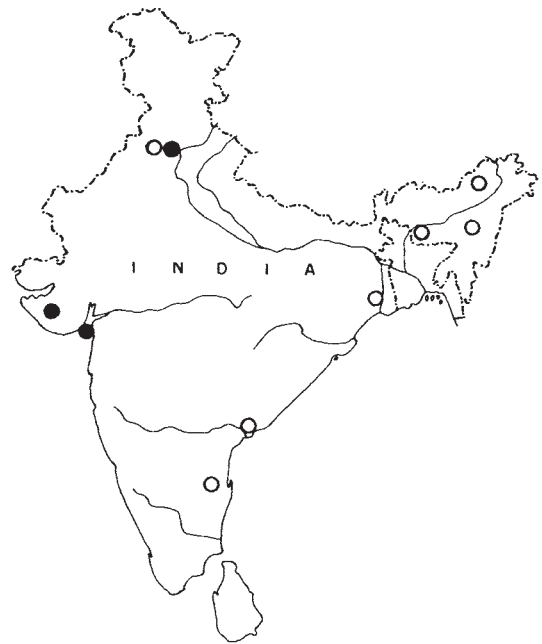


Fig. 1 Floral distribution during the Mio-Pliocene in the Indian region. ○, Miocene; ●, Pliocene.

large river valleys and swamps. The bulk of the Nagri fauna associated with *Ramapithecus* is known from Haritalyangar⁴. The ecology can be studied by correlating the extinct mammalian material including *Ramapithecus* with the flora.

Two species of *Hipparion* are known from the Nagri beds: the slender, widely occurring *Hipparion antilopinum* may have been a forest browser; the robust *Hipparion theobaldi* apparently preferred an open country environment where forest partially receded especially during the Dhokpathan-Pliocene. *Giraffokeryx*, which is closely allied to *Okapia*, seems to have been a forest dweller, but giraffes are known to prefer open grasslands with scattered trees. The doubtful tubulidentate (*Orycteropus*) could adapt to all types of habitats. The hystriid and rhizomyid rodents present in the sediments do not throw sufficient light on environment. The tragulids preferred river banks, whereas the canids and felids could adapt to varying types of habitat. Few typical gazelles are known from Nagri. Convincing evidence for a mixed type of forest vegetation accrues from the presence of dinotheres and true rhinocerotids. It is difficult therefore to draw conclusions about the ecological

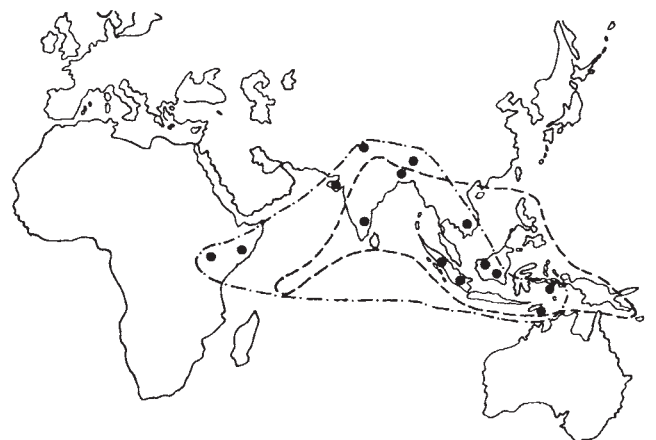


Fig. 2 Distribution of Dipterocarpaceae (modified after Chowdhury, ref. 8). ---, Distribution today; distribution during the mid Tertiary.

Ecology of the Fossil Hominoidea from the Siwaliks of India

THE ecology of the North Indian *Ramapithecus* has been the subject of recent discussion¹⁻³. In such discussion the tectonic framework and uplift of the Himalayas and Siwalik sedimentation during the Miocene must be taken into account. The Middle Miocene is usually correlated with the third major upheaval during which the Himalayas acquired their major features characterized by mountain ranges interspersed by

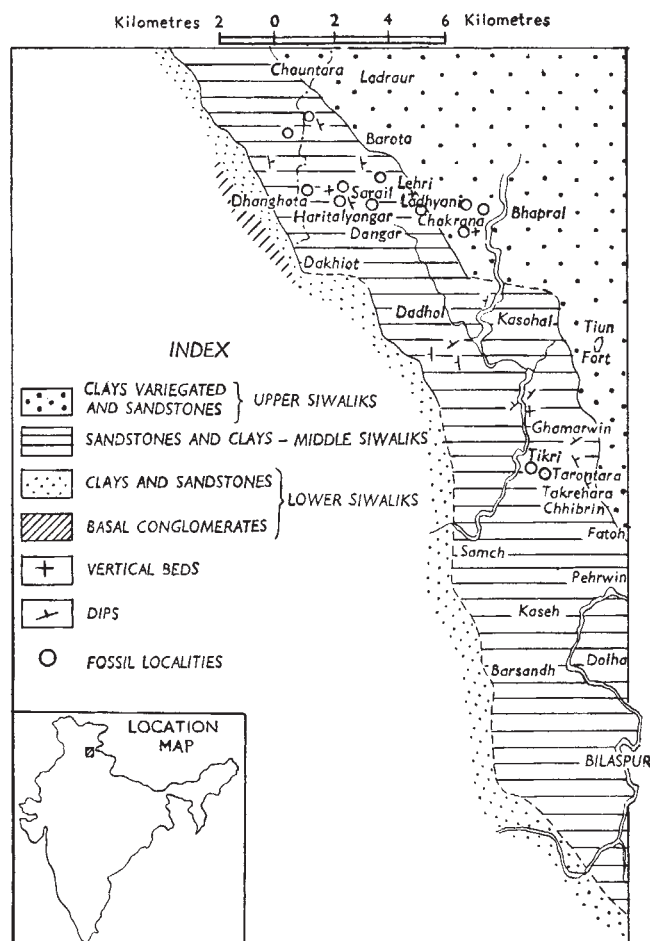


Fig. 3 Geological sketch map of the Bilaspur-Haritalyangar area.

setting of early hominids such as *Ramapithecus* without palaeobotanical evidence.

The evidence for a forest type of habitat in the Miocene lies in the presence of many dicotyledonous woods preserved in the sediments along with extinct mammalian material. Petrified leaf and wood is known from the Siwaliks⁵⁻⁸. Miocene flora of evergreen rain forest had a much wider distribution in India

Table 1 Distribution of Fossil Dicotyledon Woods in the Tertiary of India (Modified after Ramanujam⁹)

Family	Genus and species	Age
Guttiferae	<i>Kayeoxylon assamicum</i>	Upper Miocene
	<i>Calophylloseylon eoinophyllum</i>	Middle Miocene
	<i>Dipterocarpoxyylon garoense</i>	Upper Miocene
Dipterocarpaceae	<i>Dipterocarpoxyylon chowdhuryi</i>	Middle Tertiary
	<i>Shoreoxylon evidens</i>	Middle Tertiary
	<i>Anisopteroxyylon bengalensis</i>	Sub-Recent
	<i>Anisopteroxyylon jwalamukhi</i>	Miocene
	<i>Glutoxyylon burmense</i>	Upper Miocene
Anacardiaceae	<i>Glutoxyylon chowdhuryi</i>	Sub-Recent
	<i>Glutoxyylon bengalensis</i>	Pliocene
	<i>Cynometroxylon indicum</i>	Upper Miocene
Leguminosae (Caesalpinae)	<i>Pahudioxylon bankuriensis</i>	Upper Miocene
	<i>Pahudioxylon sahnii</i>	Middle Miocene
Combretaceae	<i>Terminalioxylon chowdhuryi</i>	Middle Tertiary
	<i>Terminalioxylon tertiarum</i>	Middle Miocene
Ebenaceae	<i>Ebenoxylon indicum</i>	Upper Miocene

during the mid-Tertiary (Fig. 1). *Dipterocarpoxyylon* is known from Cutch, the Siwalik Hills of Punjab and foothills region of West Bengal. Fossil woods of Dipterocarpaceae originally distributed in the Malay region are also known from East Africa⁸ (see Fig. 2). During the Miocene, *Gluta* was growing in West Bengal and Assam but is now confined to the extreme south-west coast and south Burma. The presence of the moist favouring Dipterocarpaceae and several fossil woods referable to *Mesua*, *Gluta*, *Cynometron* and *Calophyllum* in south-east Asia, including the Siwaliks, and in East Africa indicates that the climate during Mio-Pliocene was tropical with plenty of rainfall and supporting heavy forest—fossil woods and other associated floral material are usually considered to be reliable indicators of past climate. The climate seems to have been similar and more or less uniform along the foothills region of the Siwaliks from Assam to Punjab.

Leakey² asks "Was the very sparse *Ramapithecus* material from the Nagri zone actually excavated from a limited area, at a single level, in association with Lorisids and Pongids?". The Nagri Stage is represented by a thickness of 1,500 m of sediments and most of the fauna have been recovered from various sites within this formation^{10,11} (Fig. 3). Tattersall has suggested¹ that it is unlikely that the Nagri hominoids were subjected to heavy predation by social carnivores such as *Crocota* as propounded by me⁴. Professor G. H. R. Koenigswald (personal communication) has suggested the possibility of predation by crocodiles in addition to hyaenids because numerous crocodilian remains are found in abundance in the Nagri sediments. I suggest therefore that the Nagri environment was one of mixed forest interspersed with streams.

I thank Dr C. G. K. Ramanujam for helpful comments on flora.

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- 1 Tattersall, I., *Nature*, **221**, 451 (1969).
- 2 Leakey, L. S. B., *Nature*, **223**, 1075 (1969).
- 3 Tattersall, I., *Nature*, **224**, 821 (1969).
- 4 Prasad, K. N., *Palaeontology*, **7**, 124 (1964).
- 5 Sahni, B., *Monograph, Sahni Inst.*, No. 1 (1964).
- 6 Feistmantel, O., *Rec. Geol. Surv. Ind.*, **15**, 1 (1882).
- 7 Lakhanpal, R. N., *Pub. Centr. Adv. Study, Punjab*, **5** (1968).
- 8 Chowdhury, K. A., *Palaeobotanist*, **14** (1966).
- 9 Ramanujam, C. G. K., *Geol. Soc. Ind.*, Mem 2 (1968).
- 10 Pilgrim, G. E., *Rec. Geol. Surv. Ind.*, **63**, 4 (1913).
- 11 Prasad, K. N., *Pal. Ind.*, **39** (1969).

Evaluation of Compound Probabilities in Sequential Choice

SITUATIONS frequently occur in which a successful outcome depends on an individual making a correct choice at each of several more or less independent stages. The choice of mode of transport at various stages of a journey is one example. Comparable predicaments occur in professional, administrative, political and military life, and in communication networks generally. The temporal order of the several choices is not invariably a vital factor. Furthermore, the situation as a whole may have a stochastic character in that the probability of correct choice may vary from stage to stage.

We shall describe an experiment simulating this general type of situation, which clearly requires, for a successful outcome, the multiplication of probabilities. Studies¹ of preference for locating a target in an $m \times n$ array, or in a display

partitioned into concentric zones, indicate that the cells in the array or the concentric zones are not subjectively equiprobable as locations for the target. Subjects do not seem to guess, at random, the unknown location of the target. Their strategy of search rather has the character of "divining" where the experimenter has hidden it, or of locating it where they would expect it to be. Other experiments² suggest that many people, when faced with a situation involving compound probabilities, tend to add, instead of multiply, the chances at the different stages.

We may accordingly predict that in an $m \times n$ array, with an unknown target in each of the m rows, the subject's estimate of his chance of guessing all targets correctly will be exaggerated, as judged by the compound probability, n^{-m} , of locating the target. Our experiment is designed to test this prediction, and to elucidate the phenomena which the situation will generate.

The apparatus consisted of a board on which were set m rows each containing n receptacles, where m and n each took the values 2, 3, 4, 5 or 8. All the receptacles were empty except one in each row which contained a ticket. The number of separate stages therefore ranged from 2 to 8, with the chance of guessing correctly at each stage ranging from 2^{-1} to 2^{-3} .

The subjects were fifty grammar school boys aged 14-15 yr whose "intelligence" may be assumed to be at least as good as that of the average adult. A subject was given to understand that in order to win a prize he had to guess the correct location of the ticket in each row, only one guess per row being allowed. His task was to equate what he thought was the chance of winning the prize with one of a set of lotteries.

There were fourteen lotteries in all. Ten of them had 100 tickets each, the chance of drawing a winning ticket, based on the number of winning tickets in the particular lottery, being 0.01, 0.1, 0.2, 0.3, . . . , 0.9. The remaining four lotteries had 500, 1,000, 5,000 and 10,000 tickets respectively, with the corresponding chance of drawing a winning ticket, 0.002, 0.001, 0.0002 and 0.0001.

The range of values taken by the rows and the range of values of the receptacles allowed for twenty-five different situations. Each of the fifty subjects was assigned at random to five of these situations by means of randomized Latin squares. Ten subjects thus judged each $m \times n$ situation.

The amount of information actually required to locate the target is $m \log_2 n$ "bits", where m is the number of rows, which we will now call "stages", and n the number of receptacles,

which will be designated "alternatives". The chance of drawing a winning ticket in the lottery chosen by the subject we shall treat as an indirect estimate of his psychological probability (ψ) of winning a prize.

The results presented in Table 1 indicate that all values of ψ are overestimates, as judged by the compound probabilities, p , thus confirming our prediction. The magnitude of the overestimation is indicated by the ratios of ψ to p in Table 2, which suggests that the realism of the estimates is confounded by an apparent tendency to take less account of the number of stages than of the number of alternatives per stage, although an analysis of variance shows that in relation to the residual variance, both the inter-stage and inter-alternative variances are significant ($P < 0.01$).

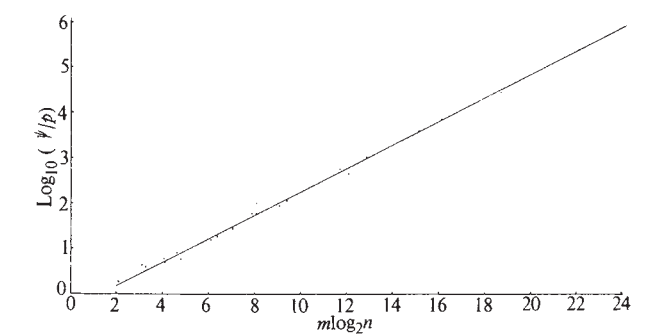


Fig. 1 Log relative overestimation plotted against the number of bits ($\log_{10} (\psi/p)$ against $m \log_2 n$). p , Compound probabilities; m , number of stages; n , number of alternatives.

This differential effect becomes clear if we plot, as in Fig. 1, the logarithm of relative overestimation, $\log_{10} \psi/p$, against the amount of information in bits, $m \log_2 n$, required to locate the target. The relation is linear, and is given by the equation:

$$\log_{10} \psi/p = 0.26 m \log_2 n - 0.31$$

(1)

This may be re-written as:

$$\psi/p = e^{(0.86 m \log_e n - 0.72)}$$

(2)

from which it follows that if we keep the number of stages constant, ψ/p is directly proportional to a power of the number of alternatives per stage, whereas if we keep the number of alternatives constant, ψ/p varies exponentially with the number of stages.

Given m and n , we can predict the mean value of ψ because

$$p = n^{-m}$$

(3)

The compound probability p is obtained by multiplying the respective probabilities of guessing correctly at each of the m stages, each of these probabilities being equal to $1/n$.

Therefore, from (2)

$$\psi = e^{-0.72} n^{-0.14 m}$$

$(e^{-0.72} = 0.49)$

(4)

In the main, therefore, the relative overestimation of ψ/p results from a subjective attenuation of the multiplicative factor, m , the number of stages. This attenuation is of the order of six-sevenths of the number of stages, within our experimental constraints. This leads us to infer that the multiplicative element in compound probability is far from being "primitive" or intuitive, which may help to explain the special difficulties which people encounter in the study of statistics.

Our interpretation is supported by similar experiments with subjects aged 9+ and 10+ yr, in which, apart from gross relative overestimation of ψ , no trends are discernible with

Table 1 Psychological Probabilities (ψ) based on Choice of Lottery *

No. of alternatives per stage	No. of stages in array					Mean
	2	3	4	5	8	
2	0.45	0.51	0.36	0.38	0.37	0.41
3	0.41	0.21	0.21	0.21	0.17	0.24
4	0.31	0.23	0.21	0.12	0.11	0.19
5	0.30	0.22	0.17	0.18	0.08	0.19
8	0.07	0.16	0.11	0.13	0.05	0.11
Mean	0.31	0.27	0.21	0.20	0.16	

* Entries in the table represent means of ten observations.

Table 2 Ratios, ψ/p , of Psychological to Compound Probabilities

No. of alternatives per stage	No. of stages in array				
	2	3	4	5	8
2	1.8	4.0	5.7	12.2	95.0
3	3.8	5.9	17.8	53.2	10^3
4	4.9	14.8	54.0	118.0	7×10^3
5	7.5	27.8	106.0	563.0	3×10^4
8	4.3	82.4	465.0	4×10^3	9×10^5

variations in the values of m and n . This too suggests that the multiplicative element is not primitive.

The method we have used involves an indirect evaluation of ψ . A more direct evaluation could be obtained by asking the subject to choose between different types of array. The utility of the choice, however, might then become an important factor.

This experiment elucidates the apparent tendency, in a variety of multi-stage choice situations, for the decision maker to misjudge the likelihood of his success, and therefore to adopt an inappropriate strategy which he will later regret.

Of historical interest in this connexion is the fact that the most subtle thinkers of ancient Greece, though greatly intrigued by the idea of the possible, especially in Stoic philosophy, never grasped combinatorial analysis, which had to wait until the sixteenth century for its development³. Aristotle himself evidently had only a small appreciation of the concept of probability. Whatever intuition of the subject he and others might have had was submerged by long established habits of thought.

The relative overestimation of compound probabilities which the experiment has revealed may be a phenomenon of considerable generality in decision and choice. If so, it merits a special designation. We propose to name it the "inertial ψ effect".

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¹ Cohen, J., Boyle, L. E., and Chesnick, E. I., *Occup. Psychol.*, **43**, 129 (1969).

² Cohen, J., and Hansel, C. E. M., *Acta Psychol.*, **13**, 357 (1958).

³ Sambursky, S., *Osiris*, **12**, 35 (1956).

Similarity Measure for Mixed Attribute Types

SUPPOSE we wish to examine the relationships among n objects (units, samples) with respect to m attributes (variates, characters, tests). Such a need arises in geology and archaeology, literary studies, medicine and all the biological sciences, particularly the taxonomy of plants and animals. I define here a numerical measure of similarity between objects that can be applied when any mixture of quantitative and qualitative attributes is involved and when observations are missing.

Quantitative data are frequently presented as an $n \times m$ matrix, X . For many purposes (for example, principal component analysis) the units are regarded as points in Euclidean space, using the Euclidean distance metric

$$d_{ij} = \sum_{k=1}^m (x_{ik} - x_{jk})^2 \quad (1)$$

as a measure of the dissimilarity between units i and j . D can be derived from the "similarity" matrix, $W = XX'$, by the relation

$$d_{ij}^2 = \omega_{ii} + \omega_{jj} - 2\omega_{ij} \quad (2)$$

Unfortunately, in many practical situations, some or all of the attributes cannot be expressed in terms of ordered quantitative values, so that W and D cannot immediately be formed. For purely qualitative data, or presence/absence data, there are many coefficients¹ for matching which measure the similarity, s_{ij} , between units i and j . It can be shown that, for many similarity measures, S is positive semi-definite (p.s.d.) so that there exists a quantitative matrix, X_s , such that $X_s X_s' = S$. Thus, S can be regarded as the W matrix for a configuration

given by X_s and therefore defines a Euclidean distance matrix by application of equation (2).

A general coefficient of similarity for mixed quantitative and qualitative attributes can be defined as follows.

If attribute k is quantitative, and scaled to have approximately unit range, let

$$s_{ijk} = x_{ik} x_{jk}$$

If attribute k is qualitative, let

$$s_{ijk} = \begin{cases} 0 & \text{when } x_{ik} \neq x_{jk} \\ 0.5 & \text{when } x_{ik} = x_{jk} \end{cases}$$

Then

$$s_{ij} = \frac{1}{m} \sum_{k=1}^m s_{ijk}$$

Thus, the measure is a combination of the simple matching coefficients and the W elements for individual attributes.

The resulting matrix, S_m , is certainly p.s.d., because any r -state qualitative attribute can be expressed as $(r-1)$ dummy quantitative variates to give an expanded data matrix, X_e , and $mS_m = X_e X_e'$. We may wish to scale or weight the attributes by factors, f_k , so that

$$s_{ij} = \frac{1}{m} \sum_{k=1}^m f_k s_{ijk}$$

This corresponds to scaling the columns of X_e and therefore the similarity matrix remains p.s.d.

The coefficient is additive over attributes or sets of attributes, which allows a recursive definition of the similarity matrix; because, if S_k is the similarity matrix for the first k attributes, and s_k is the similarity matrix for the k^{th} attribute alone, then

$$S_k = \frac{1}{k} ((k-1)S_{k-1} + s_k) \quad (3)$$

Two points should be noted. (1) In general, when quantitative data are involved, self-similarities do not equal a fixed constant, so that the units are not artificially constrained to lie on a hypersphere. There is thus no "horseshoe" effect. (2) As before, we have

$$d_{ij} = (s_{ii} + s_{jj} - 2s_{ij})^{\frac{1}{2}}$$

independent of the origin of the implicit configuration. But, when the similarity matrix itself is required (for example, for a principal component analysis), the elements of S_m must be centred; this is most easily achieved by replacing each s_{ij} by $(s_{ij} - \bar{s}_i - \bar{s}_j + \bar{\bar{s}})$, where $\bar{s}_i$ is the mean of the i^{th} row of S_m , and $\bar{\bar{s}}$ is the overall mean².

When either or both of x_{ik} and x_{jk} are unknown, s_{ijk} must be estimated. For Gower's similarity measure (first described by Smith³) s_{ijk} is set equal to the similarity based on available attribute comparisons between units i and j . This is unsatisfactory, because the m attributes are more or less independent; for example, in a human population, we would hardly be satisfied with an estimate of age similarity based on sex and blood group similarities. Furthermore, the resulting similarity matrix is not necessarily p.s.d., in which case the data cannot be represented in Euclidean space.

For the common attribute distributions, the best estimate of s_{ijk} ($= x_{ik}^2$) is given by the average of the available similarities for attribute k . This corresponds to estimating the original missing value by the mean of attribute k , based on known observations (using dummy values for qualitatives). Thus, S_m remains p.s.d.

A simple example may clarify this. Suppose we have three subjects whose sex, blood group and age are given in Table 1.

Table 1 Sex Characteristics of Three Subjects

Subject	Sex	Blood group	Age	Age/50
1	Male	A	15	0.3
2	Male	A	40	0.8
3	Female	B	60	1.2

Then, using a scaling divisor of 50 for age, we have

$$s_{11} = \frac{1}{3}(0.5 + 0.5 + 0.09) = 0.3633$$

$$s_{12} = \frac{1}{3}(0.5 + 0.5 + 0.24) = 0.4133$$

$$s_{22} = \frac{1}{3}(0.5 + 0.5 + 0.64) = 0.5467$$

so that

$$d_{12} = (0.3633 + 0.5467 - 2 \times 0.4133)^{\frac{1}{2}} = (0.0834)^{\frac{1}{2}} = 0.289.$$

Similarly, $d_{13} = 0.968$ and $d_{23} = 0.849$.

Suppose, now, that the age of subject 1 is unknown. Estimating age similarities from sex and blood group similarities gives

$$d_{12} = 0.216 \text{ and } d_{13} = 1.146$$

so that $d_{12} + d_{23} = 0.216 + 0.849 = 1.065 < d_{13}$; in other words, the triangle inequality is not satisfied. But, when we estimate the age of subject 1 to be $\frac{1}{2}(40 + 60) = 50$, or, alternatively, estimate s_{113} ($= x_{13}^2$) to be $\frac{1}{4}(s_{223} + s_{333} + 2 \times s_{233}) = \frac{1}{4}(0.64 + 1.44 + 2 \times 0.96) = 1.00$, we have $d_{12} = 0.116$ and $d_{13} = 0.825$.

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¹ Sokal, R. R., and Sneath, P. H., *Principles of Numerical Taxonomy*, ch. 6 (Freeman, San Francisco and London, 1963).

² Anderson, A. J. B., *J. Ecol.* (in the press).

³ Smith, I. W., *J. Gen. Microbiol.*, 33, 263 (1963).

Nitrogen Fixation and its Significance in Tropical Lake George, Uganda

TROPICAL lakes have been little studied although they often seem to be very productive, especially at those trophic levels exploitable by man. One such lake, Lake George (0°, 00', 29° 55' E) is a shallow lake ($\bar{z} = 2.5$ m) with an area of approximately 290 km² including the associated channel, and is one of the smaller lakes in the western arm of the Rift Valley of Africa. An important feature of the lake is the high phytoplankton standing crop of approximately 400 mg of chlorophyll a m⁻². Yet, in spite of this, there is very little inorganic nitrogen in the water. There is little seasonal variation in species composition, in the numbers of the phytoplankton and in chemical and physical parameters^{1,2}.

Enrichment experiments have shown that the phytoplankton probably suffer a semi-permanent nitrogen deficiency³. An investigation of the supply of nitrogen by direct fixation of N₂ by phytoplankton is consequently of obvious importance. N₂ fixation was measured using a ¹⁵N tracer and an acetylene reduction assay⁴⁻⁸ during wet and dry seasons representative of a full year. A value of 0.008 atom percentage excess over a biological control not exposed to ¹⁵N₂ is significant at the $P = 0.05$ level.

Table 1 Seasonal and Depth Variations of Nitrogen Fixation in Lake George

Date (1968)	Incubation depth (cm)	Organic N present (mg l. ⁻¹)	Atom % excess in sample*	Nitrogen fixed % Fixation (l. ⁻¹ h. ⁻¹ × 10 ³)	(μg l. ⁻¹ h. ⁻¹)	(mg m ⁻² h. ⁻¹)
February 2	0	2.48	0.0557	22.3	0.55	—
February 5	15	3.18	0.1070	13.4	0.43	—
February 16	0	2.82	0.2791	50.0	1.41	
	15	1.51	0.2317	41.5	0.63	
	40	3.01	0.1625	33.7	1.01	1.66
	150	2.52	0.1479	30.6	0.77	
March 5	0	4.09	0.0618	16.0	0.65	
	15	1.18	0.0457	11.4	0.13	
	40	3.96	0.0263	6.6	0.26	0.44
	150	4.01	0.0123	4.7	0.19	
March 20	0	4.14	0.0435	7.5	0.31	—
March 26	0	4.10	0.1615	24.3	1.00	
	15	3.93	0.1371	16.9	0.66	
	40	3.96	0.2353	23.5	0.93	0.89
	150	2.34	0.0377	3.8	0.09	

* After correction for partial pressure and enrichment of ¹⁵N₂ gas used.

Table 1 shows that N₂ fixation rates of 0.44–1.66 mg N m⁻² h⁻¹ varied irregularly during wet, dry and interseason weather. This contrasts with the pattern in temperate and polar lakes where pronounced peak(s) of N₂ fixation occur during the warm water period⁸⁻¹². The relative maximum rate of fixation, expressed as a proportion of the total amount of nitrogen present, was 0.05% h⁻¹ (approximately 0.6% day⁻¹). Satisfactory reasons for these irregular and continuously high rates are not known but the following points are probably influential. First, Lake George diel variations in phytoplanktonic standing crop and productivity can be greater than seasonal changes. Second, the euphotic zone is shallow (60 cm) so that the algae receive irregular amounts of light as they are circulated in and out of the zone. Thus on successive days the physiological state, previous light history and nutrient status of the phytoplankton may often have been different even when the samples were collected at the same time and place.

It is possible that in the afternoon dissolved O₂, which may reach 250% saturation, could reduce the rate of N₂ fixation^{13,14}. The frequent pronounced minima of N₂ fixation at 15 cm, which was the depth of maximum photosynthesis during much of the day, may be a direct result of high oxygen concentration, the effect of which must be quite rapid as it was found in both long and short exposure experiments.

The daily fixation against depth profiles reveals a surface maximum, a subsurface maximum at 40 cm and pronounced minima at 15 and 150 cm. This pattern, partially due to crop size, was different from the exponential decrease with depth that occurs in the English Lakes⁹ but was more like the pattern found in Tjeukemeer⁸ and Clear Lake¹⁵. Fixation at 150 cm, a region of very low light, was nevertheless appreciable, ranging from 3.8×10^{-30} % h⁻¹ (0.09 μg N l.⁻¹ h⁻¹) to 30.6×10^{-3} % h⁻¹ (0.77 μg N l.⁻¹ h⁻¹). This consistent fixation at 150 cm requires comment because this was a region with a light intensity well below the photosynthesis/respiration compensation point. The phenomenon of significant fixation in the dark was also found occasionally in the thermally stratified lakes of the English Lake District⁹ so that it would seem to be common to a wide variety of waters. Photosynthetic bacteria are present in late summer in the

anoxic hypolimnium of eutrophic Esthwaite Water, England (V. G. Collins, personal communication), and may contribute to the high rate of fixation in that lake⁹. By analogy, it is possible that photosynthetic bacteria growing at very low light intensities together with non-photosynthetic heterotrophic bacteria were contributing to fixation at 150 cm in Lake George. Results of diurnal studies of N₂ fixation in Lake George indicate that most of the fixation at 150 cm during daylight occurred in the morning when the oxygen concentration is low. Recent work showing N₂ fixation in the anoxic hypolimnia and sediments of several lakes in North America^{16,17} supports the idea of some bacterial contributions to low light fixation in Lake George. But no fixation was observed in illuminated, anoxic, H₂S-producing sediments of the lake and the anoxic zone immediately above the mud is subject to oxygen fluctuations which would deter strict anaerobes. The organism(s) responsible for fixation rates below the photic zone is thus not certain.

No species from the lake was isolated in axenic culture and tested for nitrogen fixation. Fixation was tentatively ascribed to planktonic species of *Anabaena* and *Anabaenopsis*, both of which are suspected to fix nitrogen, although there are few studies concerning pure cultures of truly planktonic blue-green algae. Both these algae were common in the lake¹, and possessed heterocysts, which are correlated with nitrogen fixation in lakes^{9,15}.

Table 2 Nitrogen Balance Sheet for Lake George—Major Features

Annual gain		Annual loss	
Source	Amount (mg)	Source	Amount (mg)
N ₂ fixation	1,280	Denitrification	?
Stream inflow*	322	Stream plankton outflow	3,180
Rainfall	277	Sedimentation	655
Hippopotamus excreta†	76-99	Commercial fish export	50-75

* Minimum values and does not include surface runoff.

† Estimated from sparse knowledge of daily herbage consumption and digestion efficiency²⁰, extrapolations from cattle urine excretion, and nitrogen analysis of faeces¹⁸.

The annual nitrogen fixation is estimated to be approximately 1,300 Mg for the whole lake, or 44 kg ha⁻¹ yr⁻¹. This quantity represents approximately 33% of the lake's annual nitrogen change and thus represents an important factor in the overall budget (Table 2). The details of calculations of nitrogen inflows and outflows from Lake George are given elsewhere¹⁸. They are based on the flow rates of the principal influents with corrections for direct rainfall and evaporation and the nitrogen content of the mean standing crop of plankton. This high percentage annual contribution is put in perspective when set against the similar value of 38% for Clear Lake, and the considerably lower value of 0.5% for the thermally stratified English lakes⁹.

The percentage for Smith Lake, Alaska, was estimated to be 5-10% (Alexander, personal communication); that for Lake Mendota, Wisconsin, is 8.5% (Fitzgerald, personal communication) while that for a Russian Lake¹⁹ was indirectly estimated to be 8%.

It would seem from our results that, in Lake George, the shortage of combined inorganic nitrogen as a nutrient for primary production puts a premium on atmospheric N₂ fixation. The daily rate at which this is carried out (0.6% of total N), although less than the highest values, is within the upper ranges reported for most other waters. More important, the relative constancy of the equatorial climate sustains this rate throughout the year, so the total N₂ fixed becomes extremely important in the nitrogen budget of the lake.

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¹ Ganf, G. G., thesis, Univ. Lancaster (1969).

² Viner, A. B., *Verh. Intern. Verein. Limnol.*, **17**, 289 (1969).

³ Viner, A. B., in *Bioenergetics and Tropical Ecosystems* (IBP/UNESCO regional symposium) (in the press).

⁴ Neess, J. C., Dugdale, R. C., Dugdale, V. A., and Goering, J. J., *Limnol. Oceanog.*, **7**, 163 (1962).

⁵ Fogg, G. E., and Horne, A. J., in *Chemical Environment in the Aquatic Habitat* (edit. by Golterman, H. I., and Clymo, R. C.), 115 (Noord-Hollandsche Uitgevers Maatschappij, Amsterdam, 1967).

⁶ Stewart, W. D. P., Fitzgerald, G. P., and Burris, R. H., *Proc. US Nat. Acad. Sci.*, **58**, 2081 (1967).

⁷ Hardy, R. W. P., Holsten, R. D., Jackson, E. K., and Burns, R. C., *Plant Physiol.*, **43**, 1185 (1968).

⁸ Horne, A. J., thesis, Univ. of Dundee (1969).

⁹ Horne, A. J., and Fogg, G. E., *Proc. Roy. Soc., B*, **175**, 351 (1970).

¹⁰ Dugdale, R. C., and Dugdale, V. A., *Limnol. Oceanog.*, **7**, 170 (1962).

¹¹ Goering, J. J., and Neess, J. C., *Limnol. Oceanog.*, **9**, 530 (1964).

¹² Billaud, V. A., *J. Fish. Res. Board Canada*, **25**, 2101 (1968).

¹³ Stewart, W. D. P., Haystead, A., and Pearson, H. W., *Nature*, **224**, 226 (1969).

¹⁴ Stewart, W. D. P., and Lex, M., *Arch. Microbiol.*, **73**, 250 (1970).

¹⁵ Horne, A. J., *Brit. Phycol. J.* (in the press).

¹⁶ Brezonik, P. L., and Keirn, M. A., *Abst. Thirty-third Ann. Meeting Limnol. Oceanog. Soc.* (Kingston, Rhode Island, 1970).

¹⁷ Howard, D. L., Frea, J. I., Pfister, R. M., and Dugan, P. R., *Science*, **169**, 61 (1970).

¹⁸ Viner, A. B., thesis, Univ. London (1970).

¹⁹ Kusnezow, S. I., *Die Rolle der Mikroorganismen im Stoff-kreislauf der Seen* (Berlin, 1959).

²⁰ Field, C. R., thesis, Univ. Cambridge (1968).

Bomb ¹⁴C in the Human Population

IN the atmosphere ¹⁴C occurs principally as ¹⁴CO₂ and is usually produced by nuclear reactions between cosmic ray neutrons and the nitrogen atoms of the air. The natural equilibrium between production and disintegration of ¹⁴C determines a part of the natural background radiation to the human population. From 1955 there has been a gradual increase of ¹⁴C in the atmosphere, the land biosphere and the ocean, as a result of nuclear tests. Although ¹⁴C was initially not regarded as an important hazard to man¹, it was later pointed out²⁻⁴ that ¹⁴C could be a source of appreciable genetic hazard in the world's population, because of its long half life (5,700 yr).

At this laboratory we have studied the ¹⁴C concentration in the human body⁵. The correspondence between ¹⁴C in the atmosphere and in the human body, mediated as it is by photosynthesis, has been confirmed in 6 yr of measurements⁶⁻⁸.

Since 1955, about two-thirds of the total nuclear energy liberated in nuclear tests has resulted from tests carried out in the atmosphere at high northern latitudes in 1961 and 1962 (ref. 9). The subsequent transfer of ¹⁴C down to the troposphere, the biosphere and the ocean has been followed in detail¹⁰⁻¹⁶. The ¹⁴C excess¹⁶ ($\delta^{14}\text{C}$) in the northern tropo-

sphere (Fig. 1) is representative chiefly of the region between 30° N and 90° N, although the curve for the southern troposphere is representative of the region from the equator to 90° S.

The model for CO₂ exchange between the various reservoirs is shown in Fig. 2, in which the CO₂ in the troposphere is in exchange with CO₂ in the stratosphere, the land biosphere and the ocean. For CO₂ exchange between the troposphere and the biosphere we share the view of Münnich (for discussion, see ref. 17), who divided the biosphere into two parts. The first (*b*₁), which consists of leaves, grass, branches, and so on, is in rapid exchange with the troposphere and is combined with this reservoir, but the larger part of the vegetation (*b*₂) has a much slower exchange rate and is combined with the humus layer.

The ocean is divided into two reservoirs, the mixed layer and the deep ocean. The exchange of CO₂ between the troposphere and the ocean occurs chiefly in the mixed layer, but according to Craig¹⁸ there is also the possibility of a direct exchange with the deep ocean. The ¹⁴C concentration in the mixed layer of the ocean is now 10 to 15% above normal^{19,20}.

Using the model of Fig. 2, we have treated the decrease of δ¹⁴C in the troposphere in a previous article²⁰. We showed that the measured variation of δ¹⁴C (*x*_{*t*}) in the troposphere is approximately reproduced by the following two-term exponential function:

$$x_t = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} \quad (1)$$

in which the parameters *A*₁, *A*₂, *k*₁, and *k*₂ depend on the various exchange coefficients. Because the errors on some of these coefficients are large, the extrapolation is uncertain and is given in the shaded area of Fig. 1.

The amount of bomb-produced ¹⁴C in the atmosphere has increased the total natural amount of ¹⁴C in nature by about 3%. According to Harkness *et al.*⁸, the production of CO₂ from fossil fuel would lower the natural ¹⁴C concentration in the atmosphere to about 16% below normal at the end of this century. It is thus reasonable that the ¹⁴C excess caused by the atomic bomb will be more than compensated for by the dilution of inactive carbon (the Suess effect).

The transfer of ¹⁴C into the human body depends on the following three factors: (1) the time between the photosynthesis in vegetational food and its consumption; (2) the diet, particularly the amount of vegetational food, and (3) the residence time of the carbon in the constituents of human tissue.

Broecker *et al.*⁶ (Fig. 1) found that it took 1 and 1.8 yr before the ¹⁴C concentration in blood and lung tissue, respectively, reached that in the atmosphere. They also found that the δ¹⁴C value of blood had a maximum time lag of 6 months behind food.

Berger and collaborators^{7,21-23} (Fig. 1) studied chiefly the metabolic turnover time of the constituents of human tissue. For this they used samples from persons who had travelled from the southern to the northern hemisphere. One result of their work was that the incorporation in these people of ¹⁴C

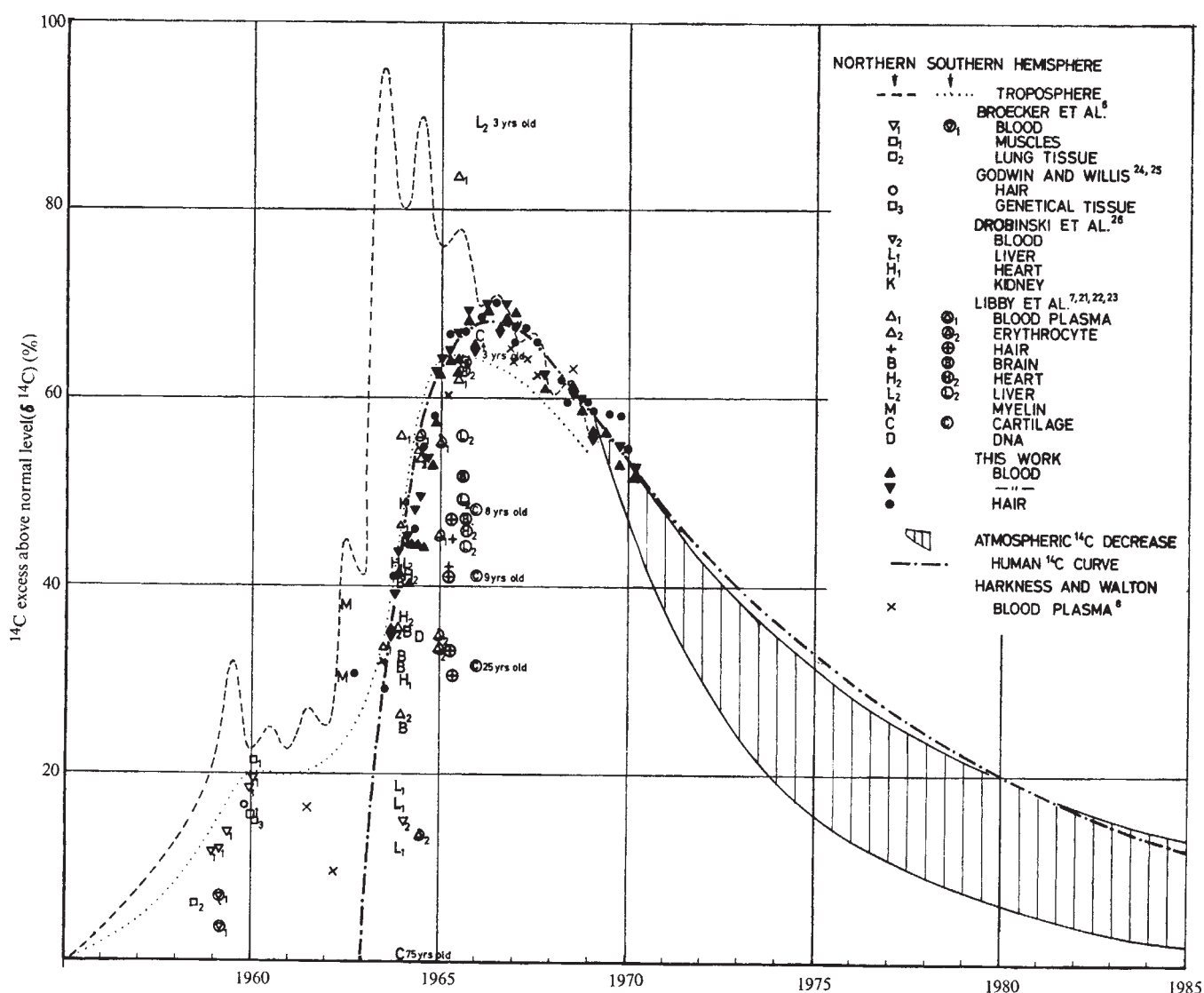


Fig. 1 Radiocarbon in the troposphere and human body.

in brain protein and lipids, liver, heart, plasma protein and erythrocyte protein was very similar to, and reflected, the atmospheric ^{14}C content present several months earlier. Collagen of cartilage was found to be metabolically inert in older persons. The concentration of ^{14}C in the human body has been studied by other workers (refs. 8, 24–26) who obtained values shown in Fig. 1.

At our laboratory the transfer of ^{14}C into the human body was studied by following the time-variation of $\delta^{14}\text{C}$ in blood and hair for three persons^{5,27} (Tables 1–3). No separation between blood plasma and erythrocyte protein was performed, and the measured ^{14}C activity is thus a mean value for the total blood samples. Fig. 1 shows that there is excellent agreement between data obtained for the blood and for the hair samples. The values of the ^{14}C concentration in blood plasma obtained by Harkness and Walton⁸ are slightly lower than ours.

Table 1 Carbon in Neck Hair, from a Boy (K.N.) Born in 1962

Time of collection	$\delta^{14}\text{C} \%$	$\delta^{13}\text{C} \text{‰}$	$\Delta^{14}\text{C} \%$
November 1962	30.7 ± 1.3		
June 1963	29.2 ± 0.8	-19.7	26.7
October 1963	41.0 ± 1.0	$-19.2 \dagger$	39.3
March 1964	46.0 ± 1.0	-18.9	44.2
July 1964	54.8 ± 1.0	$-19.2 \dagger$	52.9
October 1964	58.0 ± 0.8	-18.6	55.9
February 1965	66.9 ± 1.0	$-19.2 \dagger$	64.9
July 1965	67.2 ± 1.0	-18.6	64.5
February 1966	68.7 ± 1.0	-19.2	66.7
May 1966	70.0 ± 0.9	$-19.2 \dagger$	68.0
December 1966	65.9 ± 0.9	$-19.2 \dagger$	63.9
February 1967	67.5 ± 1.1	$-19.2 \dagger$	65.4
July 1967	65.9 ± 0.9	$-19.2 \dagger$	63.9
February 1968	61.5 ± 0.9	$-19.2 \dagger$	59.6
May 1968	60.2 ± 1.1	$-19.2 \dagger$	58.2
August 1968	61.8 ± 1.2	$-19.2 \dagger$	59.9
November 1968	59.7 ± 1.1	$-19.2 \dagger$	57.7
January 1969	58.7 ± 1.2	$-19.2 \dagger$	56.7
April 1969	58.2 ± 1.2	$-19.2 \dagger$	56.5
May 1969	58.3 ± 1.2	$-19.2 \dagger$	56.6
July 1969	58.1 ± 1.1	$-19.2 \dagger$	56.4
October 1969	54.9 ± 0.9	$-19.2 \dagger$	53.1
December 1969	54.7 ± 1.1	$-19.2 \dagger$	52.9

† Not measured (mean value).

Table 2 Carbon in Blood Samples, from a Woman (I.H.), 26 Yr Old in 1963

Time of collection	$\delta^{14}\text{C} \%$	$\delta^{13}\text{C} \text{‰}$	$\Delta^{14}\text{C} \%$
September 1963	34.9 ± 1.1	-22.0	34.0 ± 1.1
October 1963	39.3 ± 0.8	-22.2	38.5 ± 0.8
November 1963	43.6 ± 0.8	-22.7	42.9 ± 0.9
February 1964	45.6 ± 1.1	-22.0	44.7 ± 1.2
April 1964	48.1 ± 1.1	-21.7	47.1 ± 1.1
June 1964	49.6 ± 1.1	$-21.7 \dagger$	48.6 ± 1.1
July 1964	53.7 ± 1.0	-22.1	52.8 ± 1.1
November 1964	62.9 ± 0.9	-19.8	61.2 ± 0.9
January 1965	64.2 ± 0.9	-19.7	62.4 ± 0.9
March 1965	65.0 ± 0.9	-20.5	63.5 ± 1.0
May 1965	67.1 ± 1.0	-21.1	65.6 ± 1.0
September 1965	69.1 ± 0.9	-22.0	67.9 ± 1.0
November 1965	65.6 ± 0.9	-21.4	64.2 ± 1.0
March 1966	69.7 ± 0.9	-22.3	68.7 ± 0.9
July 1966	67.6 ± 1.1	-21.2	66.2 ± 1.1
September 1966	69.8 ± 1.0	-21.5	68.6 ± 1.1
December 1966	67.4 ± 1.0	-21.9	66.3 ± 1.0
September 1967	62.5 ± 0.9	$-21.7 \dagger$	61.4 ± 0.9
June 1968	60.6 ± 0.9	$-21.7 \dagger$	59.5 ± 1.0
August 1968	59.9 ± 0.9	$-21.7 \dagger$	58.8 ± 1.0
January 1969	56.0 ± 0.7	$-21.7 \dagger$	55.0 ± 0.7
September 1969	55.5 ± 1.2	$-21.7 \dagger$	54.5 ± 1.2
March 1970	52.6 ± 1.2	$-21.7 \dagger$	51.6 ± 1.2

† Not measured (mean value).

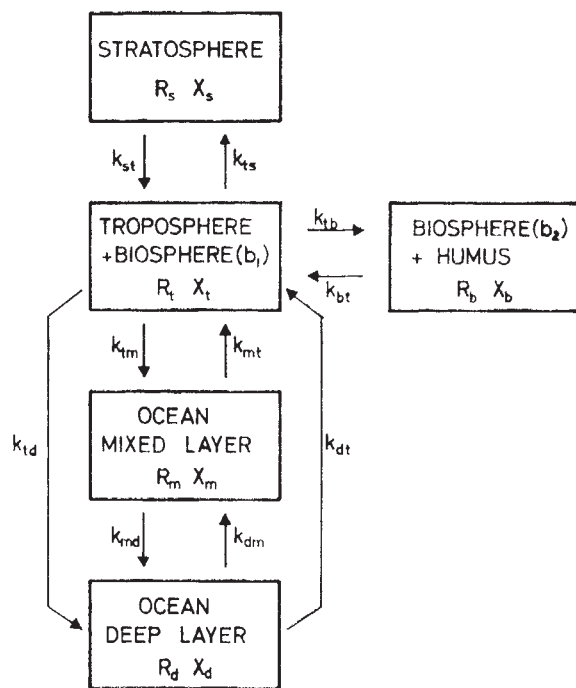


Fig. 2 Exchangeable carbon reservoirs, where: R_i , total carbon amount; X_i , ^{14}C excess; k_{ij} , exchange coefficients; i, j, a, b, m, d ($i \neq j$).

Table 3 Carbon in Blood Samples, from a Woman (A.L.), 26 Yr Old in 1963

Time of collection	$\delta^{14}\text{C} \%$	$\delta^{13}\text{C} \text{‰}$	$\Delta^{14}\text{C} \%$
September 1963	35.2 ± 0.8	-21.6	34.2 ± 0.8
November 1963	41.5 ± 0.6	$-21.7 \dagger$	40.6 ± 0.7
February 1964	40.5 ± 0.6	-20.9	39.3 ± 0.7
March 1964	44.4 ± 0.8	-22.5	43.5 ± 0.9
April 1964	44.2 ± 0.7	-23.2	43.6 ± 0.7
June 1964	44.2 ± 1.0	-22.1	43.3 ± 1.0
August 1964	53.4 ± 0.8	-21.9	52.4 ± 0.9
November 1964	57.6 ± 0.9	-20.7	56.2 ± 0.9
January 1965	62.4 ± 0.9	-19.1	60.5 ± 0.9
March 1965	64.3 ± 0.7	-20.1	62.6 ± 0.7
May 1965	63.9 ± 0.9	-21.0	62.5 ± 1.0
September 1965	68.4 ± 0.9	-22.0	67.3 ± 1.0
November 1965	65.9 ± 0.7	-21.4	64.4 ± 0.8
March 1966	69.6 ± 1.0	-22.0	68.5 ± 1.1
July 1966	67.5 ± 1.0	-21.2	66.2 ± 1.1
September 1966	68.3 ± 1.0	-20.9	66.9 ± 1.0
December 1966	69.0 ± 0.9	-20.8	67.6 ± 1.0
September 1967	60.9 ± 0.9	$-21.7 \dagger$	59.8 ± 0.9
June 1968	61.4 ± 0.9	$-21.7 \dagger$	60.3 ± 0.9
August 1968	58.8 ± 0.9	$-21.7 \dagger$	57.7 ± 0.9
January 1969	56.6 ± 0.7	$-21.7 \dagger$	55.6 ± 0.7
May 1969	56.4 ± 1.0	$-21.7 \dagger$	55.4 ± 1.0
September 1969	53.0 ± 1.0	$-21.7 \dagger$	52.0 ± 1.0
March 1970	51.6 ± 1.1	$-21.7 \dagger$	50.6 ± 1.1

† Not measured (mean value).

The blood and hair data are almost representative for persons living in the northern hemisphere. Because $\delta^{14}\text{C}$ in the southern troposphere at present lags behind that of the northern troposphere by about 1 yr, there should also be a similar lag for $\delta^{14}\text{C}$ in the human populations of the respective hemispheres. After about 1970, the ^{14}C concentrations in people in the northern and southern hemispheres will be similar, and equal to those in the troposphere. Fig. 1 shows that $\delta^{14}\text{C}$ (x_H) in the human body appears as a pulse, delayed with respect to that of the atmosphere. The observed values

for x_H can be fitted reasonably well by the following two-term exponential function:

$$x_H = 108 (e^{-0.1t} - e^{-0.75t}) \quad (2)$$

The coefficients in this function were determined by a least mean squares method, using the upper limits of the measured values for ^{14}C in the human body in the period from 1963 to 1970, and extrapolated values in the troposphere in the period from 1970 to 2000. The upper limit values were chosen because there was some excess ^{14}C before 1963 which should also be considered. There is also a tendency for the blood and hair data during the last 2 yr to correspond with the upper limit of the shaded area in Fig. 1. Function (2) was simplified by assuming that all previous nuclear tests occurred within a short time interval, and that the ^{14}C increase in the human population started in about January 1963.

The first term in the brackets of equation (2) indicates that the excess ^{14}C in the human body has a mean lifetime of about 10 yr and the second term that ^{14}C enters the human body with a mean delay time of about 1.4 yr after production in the atmosphere. The latter value is probably accurate to within 30% and agrees with previous estimates^{6,7}.

The hazard to the human population from artificial radio-carbon arises largely from inventory radiation of the body. Natural ^{14}C contributes with a certain dose rate, r_0 , as a result of its decay rate of about fourteen disintegrations per min per gram of carbon. The average value of r_0 is about 1.06 mrad yr⁻¹. The dose from natural ^{14}C is distributed as follows: 1.64 mrad/yr in the bones, 1.15 mrad/yr in the cells lining bone surfaces and 0.71 mrad/yr in bone marrow and soft tissue. Applying function (2), the dose D_1 absorbed in the human body during a time t can be calculated from the formula:

$$D_1 = 1.08 r_0 \int_0^t (e^{-0.1t} - e^{-0.75t}) dt \quad (3)$$

For a period of about 30 yr the total radiation dose from this source will be $9r_0$. We thus obtain a total radiation dose of 16 mrad to bone, 11 mrad to cells lining bone surfaces and 7 mrad to bone marrow and soft tissue. The genetic hazard is caused by the latter. That dose constitutes about 10% of the total gonad dose from all radioactive fallout. Purdom⁴ pointed out, however, that the actual gonad dose is somewhat larger because of a transmutation process in the DNA molecule, in which the decaying ^{14}C atoms are replaced by nitrogen atoms. Purdom assumed that the biological damage from the transmutation was equal to that from β -radiation.

The amount of artificial ^{14}C in the human body at about the year AD 2000 will constitute about 3% of the total amount of ^{14}C . This isotope has a half-life of 5,700 yr, and several scientists^{2,3,9,28} think that it would therefore cause a most serious genetic threat. The long term radiation dose can be calculated from the formula

$$D_2 = 0.03r_0 \int_0^t e^{-0.000125t} dt$$

The total radiation doses ($D_1 + D_2$) which will be received by the bone cells, the cells lining bone surfaces, and the bone marrow and soft tissue in the next 10,000 yr will be 410, 290 and 180 mrad, respectively. These doses, which are in agreement with values given in a United Nations report⁹ (page 45), are more important than those from all other radioactive fallout. We question, however, the value of the long term radiation dose (D_2) because, as previously mentioned, the use of fossil fuel might reduce the ^{14}C concentration in man below normal. We are of the opinion that the only ^{14}C hazard from previous tests which should be taken into account is attributable to a total genetic dose (D) of the order of 10 mrad, received in a period of about 30 yr. This dose is, however,

negligible compared with the dose received from natural sources, which constitutes about 100 mrad per yr.

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- ¹ Libby, W. F., *Science*, **123**, 657 (1956).
- ² Pauling, L., *Science*, **128**, 3333 (1958).
- ³ Sakharov, A. D., *Soviet Scientists on the Danger of Nuclear Tests*, 39 (Foreign Languages Publishing House, Moscow, 1960).
- ⁴ Purdom, C. E., *New Scientist*, **298**, 255 (1962).
- ⁵ Nydal, R., *Nature*, **200**, 212 (1963).
- ⁶ Broecker, W. A., Schulert, A., and Olson, E. A., *Science*, **130**, 331 (1959).
- ⁷ Libby, W. F., Berger, R., Mead, J. F., Alexander, G. V., and Ross, J. F., *Science*, **146**, 1170 (1964).
- ⁸ Harkness, D. D., and Walton, A., *Nature*, **223**, 1216 (1969).
- ⁹ *Rep. UN Sci. Comm. Effect of Atomic Radiation*, No. 14 (A/5814) (United Nations, New York, 1964).
- ¹⁰ Münnich, K. O., and Roether, W., *Proc. Monaco Symp.*, 93 (Vienna, 1967).
- ¹¹ Bien, G., and Suess, H., *Proc. Monaco Symp.*, 105 (Vienna, 1967).
- ¹² Rafter, T. A., *NZ J. Sci.*, **8**, 4, 472 (1965).
- ¹³ Rafter, T. A., *NZ J. Sci.*, **11**, 4, 551 (1968).
- ¹⁴ Young, J. A., and Fairhall, A. W., *J. Geophys. Res.*, **73**, 1185 (1968).
- ¹⁵ Lal, D., and Rama, J., *Geophys. Res.*, **71**, 2865 (1966).
- ¹⁶ Nydal, R., *J. Geophys. Res.*, **73**, 3617 (1968).
- ¹⁷ Nydal, R., *Symp. on Radioactive Dating and Methods of Low-Level Counting*, UN Doc. SM 87/29 (International Atomic Energy Agency, Vienna, 1967).
- ¹⁸ Craig, H., *Second UN Intern. Conf. on the Peaceful Uses of Atomic Energy*, A/CONF. 15/P/1979 (June 1958).
- ¹⁹ Rafter, T. A., and O'Brien, B. J., *Proc. 12th Nobel Symp.* (Almqvist and Wiksell, Uppsala, 1970).
- ²⁰ Nydal, R., and Lövsseth, K., *CACR Symp.* (Heidelberg, 1969); *J. Geophys. Res.*, **75**, 2271 (1970).
- ²¹ Berger, R., Fergusson, G. J., and Libby, W. F., *Amer. J. Sci., Radiocarbon Suppl.*, **7**, 336 (1965).
- ²² Berger, R., and Libby, W. F., *Amer. J. Sci., Radiocarbon Suppl.*, **8**, 467 (1966).
- ²³ Berger, R., and Libby, W. F., *Amer. J. Sci., Radiocarbon Suppl.*, **9**, 477 (1967).
- ²⁴ Godwin, H., and Willis, E. H., *Amer. J. Sci., Radiocarbon Suppl.*, **2**, 62 (1960).
- ²⁵ Godwin, H., and Willis, E. H., *Amer. J. Sci., Radiocarbon Suppl.*, **3**, 77 (1961).
- ²⁶ Drobinski, jun., J. C., La Gotta, D. P., Goldin, A. S., and Terril, jun., J. G., *Health Phys.*, **11**, 385 (1965).
- ²⁷ Nydal, R., and Lövsseth, K., *Nature*, **206**, 1029 (1965).
- ²⁸ Pauling, L., *Les Prix Nobel*, 296 (1963) (Nobelstiftelsen, Stockholm, 1964).

Cosmic Ray Flashes in the Eye

THE observations by Apollo astronauts of light flashes in the eye during lunar flights have been interpreted by Fazio *et al.*¹ as Čerenkov radiation. These authors have also considered the possibility of direct stimulation of the retinal cells by the passage of cosmic rays. I wish to show that the observed effects can also be interpreted as scintillations produced in the eye lens by the passage of multiply charged cosmic rays.

It has been found in experiments here that scintillations are produced by alpha particles of 5.3 MeV in eye lenses from freshly killed bullocks. The polonium alpha source was deposited on the tip of a silver wire which was then inserted into the lens. The lens and incorporated alpha source were mounted between a pair of photomultipliers operated in coincidence and easily detectable scintillations were observed. The single electron pulse spectrum was measured by established techniques²; using the manufacturer's figure of 10% for the

quantum efficiency of the photocathode, the measured maximum pulse height of the scintillations and the known geometry of the experimental arrangement, a figure of 1,000 photons was calculated for the approximate size of the maximum scintillations produced by 5.3 MeV alpha particles along their track length of 40 μm in the eye lens. The higher specific ionization produced by M and H group nuclei in the primary cosmic radiation should produce much larger scintillations for comparatively low particle energies of less than 1 GeV.

Light from such scintillations is of course distributed over the whole interior of the eyeball and it is necessary to postulate some focusing mechanism for some of this light to account for the point flashes reported by astronauts. The water-air interface at the front surface of the cornea will act as a partially reflecting concave mirror for light coming from within the eye. When the eyelid is not in optical contact with the cornea, the percentage of light reflected back into the eye is about 2% and scintillations in the lens will be focused to give an image on the retina. The focusing will be sharp only for certain points within the eye lens and the amount of light reflected back will be limited by the aperture of the pupil of the eye.

For a fully dilated pupil, approximately 0.15% of the light produced in a scintillation in the eye lens will be reflected to give an image on the retina and for a scintillation track of length 60 μm the light reflected will fall within an area of diameter 300 μm on the retina. Taking ten photons as the minimum detectable, a scintillation size of 7,000 photons is therefore required to give a detectable flash. In general, if a particle has sufficient energy to travel through several mm of the eye lens two points along the scintillation track will be brought to sharp focus on the retina, thus producing a double flash. If the eye is closed, reflexion will take place at the inside surface of the eyelid. The partially diffuse nature of this reflexion will mean that the flashes should appear as blobs, though this will be compensated to some extent by the improvement in the fraction of light reflected at this surface.

Scintillations large enough to be visible will be produced only by particles of high charge and relatively low energies (less than 1 GeV). Such particles are below the geomagnetic cut-off for latitudes such as have been used in manned Earth orbiting satellites and it is not to be expected that visible flashes would be reported in such flights. Measurements have not yet been made of the flux of low energy primary cosmic radiation in the regions well away from the Earth, so it is not possible to calculate an expected flash rate. However, taking a figure of 1 per min as the flash frequency observed by the astronauts leads to a flux of particles producing visible scintillations of $7 \text{ m}^{-2} \text{ s}^{-1} \text{ sr}^{-1}$, which seems to be of the right order of magnitude.

The number of visible flashes should be considerably increased if the reflexion coefficient at the front surface of the cornea is improved. This can be done by the use of contact lenses which are silvered on the front surface. As D'Arcy and Porter³ have reported visible flashes seen by dark adapted observers, an attempt was made to see if this effect was enhanced by the wearing of a contact lens aluminized on the front surface. So far it has been possible to do this only with one observer, but flashes of two different sorts have been reported with a low total frequency of about one every 20 min. These flashes were described either as balls of light or as a cloud of light. It is suggested that attempts to confirm these observations might be made in high altitude flights, where there should be an appreciable flux of the primary radiation.

I thank Dr S. McMurphy for wearing an aluminized contact lens and reporting on the observed effects, and Dr J. Fitzgerald for depositing the reflecting aluminium on the lens used.

The recent article by Charman *et al.*⁴ on the effects observed when 14 MeV neutrons interact in the eye tends to support the scintillation hypothesis because knock-on protons with energies of this order could produce enough photons to be just detectable after reflexion to a dark adapted retina. The streaks reported when the neutron beam enters the eyeball laterally are to be

expected since a scintillation track of finite length perpendicular to the lens axis will produce a finite line image on the retina. Knock-on protons produced by 3 MeV neutrons would not, on the basis of the figures quoted earlier, produce visible flashes. This accords with the results obtained by Charman *et al.*⁴.

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¹ Fazio, G. G., Jelley, J. V., and Charman, W. N., *Nature*, **228**, 260 (1970).

² Delaney, C. F. G., and Walton, P. W., *Nuclear Instruments and Methods*, **25**, 353 (1964).

³ D'Arcy, F. J., and Porter, N. A., *Nature*, **196**, 1013 (1962).

⁴ Charman, W. N., Dennis, J. A., Fazio, G. G., and Jelley, J. V., *Nature*, **230**, 522 (1971).

Structure of Acetylcholine

IN a recent letter, Chothia and Pauling¹ comment on our paper dealing with the determinants of specificity at cholinergic synapses². They correctly point out that we do not define the conformation of acetylcholine which is responsible for its action at nicotinic sites. Moreover, they present a calculation to show that because the acetylcholine ester grouping is not planar in the conformation shown in the figures, it represents only a negligible proportion of the molecules in solution. From this they conclude that this model of acetylcholine is not relevant to the roles of the molecule as a neurotransmitter.

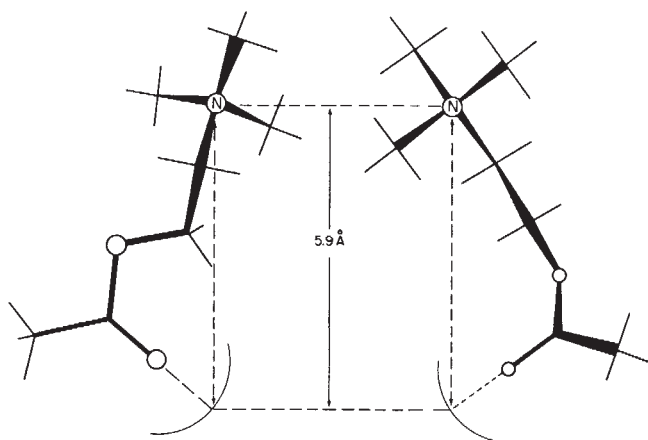


Fig. 1 The drawing used to demonstrate that acetylcholine can meet the proposed requirements for nicotinic activity in our paper is shown here on the right. In the conformation shown on the left the ester group is planar and the requirements are nonetheless fulfilled.

Our analysis is based exclusively on the spatial disposition of functional groups in cholinergic drugs which have either rigid structures or limited degrees of conformational freedom. For each of these drugs we specify and justify a specific conformation. In contrast, we suggest no specific conformation for acetylcholine, and the structure of acetylcholine represented in the diagrams was not intended to imply one. It was meant to demonstrate simply that acetylcholine can fulfil the requirements specified by the rigid drugs, which for the nicotinic receptor is a distance of 5.9 Å between the charge and H-bond. Acetylcholine can meet these restrictions in a very large number

of conformations that maintain the atoms in the ester grouping coplanar (Fig. 1). The large number of conformations can be appreciated by recalling that there is essentially free rotation about the O—C bond, that rotation about the bond between the α and β carbons also occurs readily³ and that hydrogen bonds involving oxygen as the acceptor have few, if any, geometric restrictions⁴.

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¹ Chothia, C., and Pauling, P., *Nature*, **229**, 281 (1971).

² Beers, W. H., and Reich, E., *Nature*, **228**, 917 (1970).

³ Burgen, A. S. V., *Ann. Rev. Pharmacol.*, **10**, 7 (1970).

⁴ Pauling, L., *The Nature of the Chemical Bond*, third ed. (Cornell University Press, Ithaca, 1960).

Presence and Function of Disclinations in Surface Coats of Unicellular Organisms

If a cell which is topologically a sphere is covered with a coat composed of identical units arranged to form a surface crystal, this crystal necessarily¹ contains screw disclinations of total strength $+2$ complete rotations. Harris and Scriven² draw attention to the micrograph of a marine bacterium, *Nitrosomonas*, published by Watson and Remsen³, on the cover of *Science*, showing a coat of apparently spherical units in close packing. They say that intrinsic disclinations are strongly indicated. We have undertaken further analysis of the disclination structure of this coat.

The structure clearly contains a grain boundary which terminates in the visible part of the coat. Such a termination is a partial disclination. We can show that the visible part of the coat, including the two regions which have apparently been removed in preparation, contains just two disclinations each of strength $+1/6$. Fig. 1 reproduces the micrograph of Watson and Remsen, with the addition of lines indicating the continuous variation of a lattice direction in the crystal. To analyse the disclination structure, a point was taken that lay between the termination of the grain boundary and the margin of the adjacent missing region. The lattice direction at this point which lies roughly parallel to the long axis of the photograph was taken as the reference direction; this was also assumed to be the long axis of the organism. From this point, two circuits were described, each encircling one of the missing regions counter-clockwise. The lattice direction followed continuously round the circuit has rotated by $\pi/3$ counter-clockwise when the circuit closes. Each circuit therefore contains screw disclinations of total strength $+1/6$. One disclination is dissociated, and one of its partial disclinations appears as the termination of a grain boundary; the other disclination lies completely within the region which has been removed in preparation.

A disclination of strength $(6-n)/6$ has n -fold rotational symmetry. Thus the addition of two such disclinations, one at each pole, would account for the necessary total strength $+12/6$ and would fit an assumed n -fold symmetry of the cell. There are exactly two values for n that imply disclinations all of the same strength: $n=5$, with a disclination of strength $+1/6$ at each pole, and $n=6$ with no disclinations at the poles. The case $n=7$ requires fourteen disclinations of strength $+1/6$ and two of strength $-1/6$; all other possible values of n require disclinations at the poles with strengths of magnitude greater than the minimum. Dislocation glide provides a

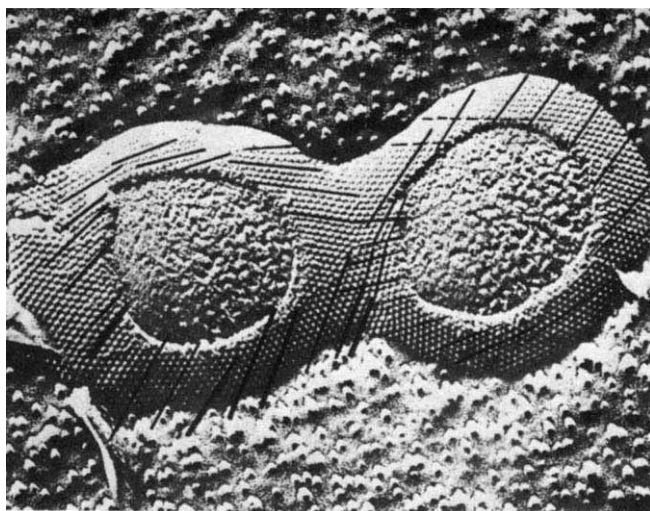


Fig. 1 Micrograph of the coat of *Nitrosomonas* with additional lines indicating the continuous variation in the lattice direction in the crystal.

mechanism whereby disclinations can dissociate into disclinations of lower strength and move to lower the total strain energy². Therefore one expects all values of n , other than 5 and 6, to be unlikely. In the micrograph there is no evidence for flattening at the poles as is required if $n=6$. Thus one is left with the most probable result that $n=5$, that is, that there are twelve disclinations each of strength $+1/6$, including one at each pole.

While the presence of disclinations in coats of this kind is a geometrical necessity, they have no obvious direct biological function. They can, however, act as sources of edge dislocations², and edge dislocations are the natural growth points in a surface crystal⁴. This suggests the intriguing possibility of the chemotherapy of diseases associated with the growth of cells having membranes of this kind by the mechanism known to metallurgists as Cottrell locking. A suitable small molecule will be incorporated into the structure at the core of an edge dislocation in preference to an additional unit of the membrane. Further growth at this point is stopped.

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¹ Harris, W. F., in *Fundamental Aspects of Dislocation Theory* (edit. by Simmons, J. A., et al.) (National Bureau of Standards, Washington, DC, in the press).

² Harris, W. F., and Scriven, L. E., *J. Appl. Phys.* (in the press).

³ Watson, S. W., and Remsen, C. C., *Science*, **163**, 685 (1969).

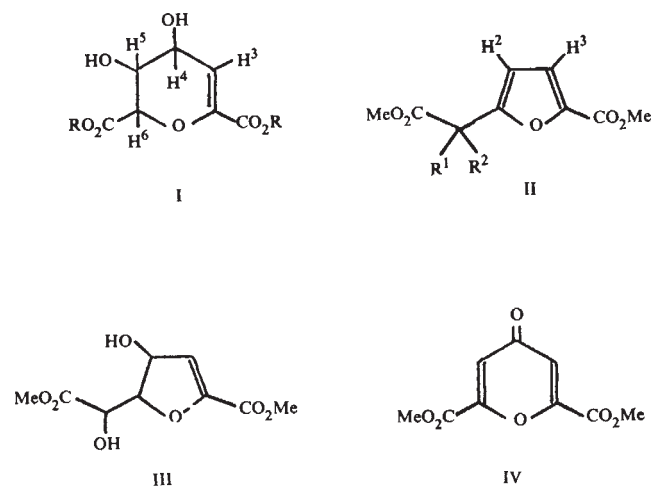
⁴ Harris, W. F., and Scriven, L. E., *Nature*, **228**, 827 (1970).

Daucic Acid and its Occurrence in Plants

DURING anion-exchange chromatography of extracts of biological materials, acidic non-nucleotide contaminants of the nucleotide fraction have often been encountered. They are usually identified by their characteristic ultraviolet absorption maxima. Thus the leaves of maize (*Zea mays*) were shown to

contain chelidonic acid¹, the leaves of wheat (*Triticum sativum*) *trans*-aconitic acid (unpublished results of A. J. K., and M. J. Cornelius) and certain animal tissues ascorbic acid². These compounds were present in sufficient quantities to interfere with ultraviolet analysis of the chromatographic fractions. During a study³ on the free nucleotides of the root of carrot (*Daucus carota*) another contaminant was observed with a maximum at 240 nm. The spectrum did not change with pH until decomposition occurred in highly acid media. The contaminant was eluted with adenosine diphosphate which indicated a strong or multibasic acid.

Bulk quantities of this acid, conveniently named daucic acid, were isolated from carrots (preferably mature) by extraction of the pulped roots with hot water. After the removal of solid material, the acid, together with nucleotide and polysaccharide material, was adsorbed on activated charcoal at pH 2. The charcoal was washed with water and the acids desorbed with 0.2 M ammonium hydroxide. The solution was concentrated and the low molecular weight ammonium salt (located by the 240 nm ultraviolet absorption), was separated from nucleotide and polysaccharide material by gel filtration on 'Sephadex G 10'. Further purification was achieved by ion exchange chromatography⁴ on 'Dowex-1 X 4' (200–400 mesh). The free acid, liberated using the hydrogen form of a cation-exchange resin, was methylated with diazomethane in methanol-ether. By this procedure, 12.7 kg of carrot roots yielded 460 mg of the diester.



Dimethyl daucate (I; R=Me) had a melting point (in ethyl acetate–light petroleum (boiling point 60–80° C)) of 130–131° C, an $[\alpha]_D^{25}$ of -102° (c, 0.9 in acetone), a mass spectrum, M^+ 232, with significant peaks at m/e 169, 155, 145 (100%), 139 and 127, a λ_{max} (in ethyl alcohol) at 242 nm (ϵ 5,600); ν_{max} (in 'Nujol') at 3,500, 1,740, 1,720 and 1,650 cm^{-1} and τ (in $CDCl_3$) 3.96 (1H, m, H-3), 5.34 (1H, m, H-6), 5.49 (1H, m, H-4), 5.70 (1H, m, H-5), 6.20 (3H, s, OMe), 6.23 (3H, s, OMe), 6.72 (2H, m, OH). [Found, C, 46.4; H, 5.04; $C_9H_{12}O_7$ requires C, 46.6; H, 5.2%.] INDOR decoupling experiments⁵ gave $J_{3,4}=3$ Hz, $J_{4,5}$ indeterminate, $J_{4,6}=1$ Hz, $J_{3,5}=1$ Hz, $J_{3,6}=0$, $J_{5,6}=2$ Hz. These assignments were supported by a study of the diacetate⁷ of the diester of $\tau(C_6D_6)$ 3.98 (1 H, m, H-3), 4.15 (1 H, m, H-5), 4.37 (1 H, m, H-4), 5.65 (1 H, m, H-6), 6.56 (6 H, s, OMe), 8.21 (6 H, s, COCH₃). INDOR experiments⁴ gave $J_{3,4}=2.6$ Hz, $J_{4,5}=4.4$ Hz, $J_{4,6}=0.8$ Hz, $J_{3,5}=1.5$ Hz, $J_{3,6}=0$, $J_{5,6}=1.8$ Hz.

The diester (I; R=Me) was treated with dry hydrogen chloride in methanol to give a 40% yield of the furan (II; R¹=OH, R²=H) with a melting point (in ethyl acetate–light petroleum (boiling point 60–80°)) of 134–135°, a mass spectrum, M^+ 214, with significant peaks at m/e 183, 155 (100%) and 122,

an $[\alpha]_D^{25}$ of $+79^\circ$ (c, 0.2, acetone), a λ_{max} (in ethyl alcohol) at 256 nm (ϵ 16,600), ν_{max} ($CHCl_3$) at 3,550, 1,740, 1,720 and 1,600 cm^{-1} and $\tau(CDCl_3)$ 2.93 (1 H, d, J=4 Hz, H-3), 3.58 (1 H, d, J=4 Hz, H-2), 4.80 (1 H, s, α -H), 6.16 (3 H, s, OMe), 6.23 (3 H, s, OMe), 6.74 (1 H, br. s, exchangeable with D₂O, OH). The furan (II; R¹=OH, R²=H) was oxidized with selenium dioxide in refluxing xylene to give, in high yield, the optically inactive ketofuran (all new compounds have been analysed by micro or mass spectral analytical techniques). (II; R¹, R²=O), m.p. (ethyl acetate) 115–116°, ν_{max} ($CHCl_3$), 1,735, 1,685 cm^{-1} , λ_{max} (EtOH), 293 nm (ϵ 13,000), mass spectrum M^+ 212, with significant peaks at m/e 181, 153 (100%) and 140, $\tau(CDCl_3)$ 2.20 (1 H, d, J=4 Hz, H-2), 2.63 (1 H, d, J=4 Hz, H-3), 6.45 (3 H, s, OMe), 6.60 (3 H, s, OMe). The ketofuran was further degraded by oxidation with alkaline hydrogen peroxide to furan-2,5-dicarboxylic acid. The dimethyl ester of this was identical in all respects to authentic material⁶.

This correlation established the structure of the methanolysis product of the daucic ester as (II; R¹=OH, R²=H). This could have arisen from either the dihydropyran structure (I, R=Me) or the dihydrofuran isomer (III). The nuclear magnetic resonance evidence favours structure I and this was confirmed chemically by oxidation of daucic acid methyl ester with chromium trioxide in pyridine to dimethylchelidonate (IV) (40% yield) which was identical in all respects with authentic material. The furanoid compounds (II; R¹, R²=O) and racemic compounds (II, R¹=OH, R²=H) were synthesized by conventional methods⁷ and found to be identical in all respects to the naturally derived compounds except for the optical activity of the naturally derived (II, R¹=OH, R²=H). The stereochemistry of daucic acid will be discussed in another report.

Daucic acid has been detected in plants belonging to various other families, in wheat, sugar beet (*Beta vulgaris*), sunflower (*Helianthus annuus*) and tobacco (*Nicotiana tabacum*), and would seem to be widely distributed. The possible relationship to primary metabolic processes is being investigated.

We thank Mr P. N. Jenkins for conducting INDOR experiments, Mr M. J. Cornelius for help with the extraction procedures and Professor J. Edelman for his interest. B. D. B. acknowledges a CAPS award from the Science Research Council and Shell Research Ltd.

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¹ Atkinson, M. R., and Eckermann, G., *Aust. J. Biol. Sci.*, **18**, 437 (1965).

² Bengtsson, L. P., Deutsch, A., and Nilsson, R., *Acta Obstet. Gynec. Scand.*, **43**, 381 (1964).

³ Leaver, C. J., thesis, Univ. London (1966).

⁴ Keys, A. J., *Biochem. J.*, **108**, 1 (1968).

⁵ Kowalewski, V. J., de Kowalewski, D. G., and Ferrá, E. C., *J. Mol. Spectrosc.*, **20**, 203 (1966).

⁶ Yoder, P. A., and Tollens, B., *Ber.*, **34**, 3446 (1901).

⁷ Gagnaire, D., and Monzeglio, P., *Bull. Soc. Chim. Fr.*, 474 (1965).

⁸ Shmagina, N. N., and Moshkin, P. A., *Plasticheskie Massy*, **58** (1965) [*C. A.*, **62**, 16168e (1965)].

⁹ Chakravarti, S. N., and Swaminathan, M., *J. Ind. Chem. Soc.*, **11**, 715 (1934).

BOOK REVIEWS

The Academic Profession

The British Academics. By A. H. Halsey and M. A. Trow. (Society Today and Tomorrow.) Pp. 560. (Faber: London, May 1971.) £5.

"It is virtually impossible that any professor should make the conduct and regulation of his faculty the principal occupation of his life. I myself am a practising barrister—my two immediate predecessors were beneficed clergymen." This is the evidence, before the Royal Commission on Cambridge in 1852, of Henry Main, twenty-third professor of civil law. His evidence was not anomalous: the Royal Commission on Oxford, sitting at the same time, wrote that it was desirable that a university professorship should become "a recognized profession". By 1952 there were some 11,000 professional university teachers in Britain. Today there are more than 30,000: and a graph in Halsey and Trow's book (page 140) predicts an academic profession of some 50,000 by 1980. On this prediction about one in eight hundred of the estimated working population of the United Kingdom would be a university teacher!

So the academics of Britain certainly deserve authoritative and objective study. Halsey and Trow have now provided this study, with a clarity and perception unmatched by any previous writers on the subject. It was not an easy task, for the profession is curiously ambivalent. Its members have a dual loyalty: on one hand, to the "guild" (for want of a better word) of chemists or historians or economists on whose esteem their status in the profession depends; on the other hand, to their avocation to teach in a faculty of the university. Critics of the profession commonly assume that loyalty to the guild takes precedence over loyalty to the student. But it is a profession widely misunderstood, for a simple reason. A lawyer, a doctor, a clergyman, are professionally in touch with ordinary citizens every day. A professor of (say) pure mathematics can achieve an international reputation within his guild without having communicated, professionally, with any except other pure mathematicians. This important book, if people will take the trouble to read it, will go far toward dispelling misunderstanding.

It would be unfair on the authors for a reviewer to try to summarize 560 pages of statistical data and closely argued analysis. Suffice it to say that the book, though expensive even by modern standards, is one which those concerned with decision-making in universities cannot afford to be without.

For, as the authors say: "The government is the final arbiter of numbers and money but the university teachers themselves are the managers of expansion. Their assumptions and preoccupations are therefore crucial". And the assumptions and preoccupations of these teachers "shape thousands of unpublished decisions made in colleges and committees, and will continue to influence the rate and form of change in the 1970s". Halsey and Trow, whose views on the sociology of higher education have already won worldwide respect, have painstakingly analysed the motives and prejudices of the academics taking part in the great debate between elitists and expansionists.

After an introduction to "the English idea of a university" (it would be churlish, when the book is already so long, to wish that there had been more about the Scottish idea) the book anatomizes the academic profession (including an entertaining section in which ex-vice-chancellors will wryly recognize their image) into its statistical components: age-structure, pecuniary rewards, social origin and education, and the differentials in emolument and status which still, apparently, persist between Oxford and Cambridge on one hand, and civic universities on the other. The authors then turn to their main theme, which is the attitude of academics toward the expansion of universities in Britain. It is a theme of critical importance. Unless technological civilization collapses, mass higher education is inevitably coming to Britain; any government, left or right, is committed to financing it. But how the finance will be apportioned between university education, as we now understand it, and other forms of higher education (either in universities or elsewhere) is not yet decided. Through the "crypto-dirigisme" of the purse, the University Grants Committee, or even the Department of Education and Science, may—probably will—influence this apportionment. But in the long run it is the academics themselves who will determine the educational consequences, as surely as doctors in the health service determine diagnosis and treatment. So to ask how a university teacher's education, social origins, political persuasion, affects his views on university expansion and on the balance between teaching and research is to ask a paramount question. This is the question which Halsey and Trow ask, and answer, for Britain in the late 1960s.

To appreciate their findings in perspective, one must read the book. But in a review for a journal read chiefly by natural scientists it is desirable to offer some reassurance about the methodo-

logy and style of a book written by two social scientists. As for methodology, I yield to none in my scepticism about conclusions drawn from sociological questionnaires, and this book is full of tables compiled from replies to questionnaires. But Halsey and Trow followed up their enquiries by intensive interviews. Their experience and objectivity as interviewers are such that the natural scientist's natural suspicions can be put at rest. Another reasonable misgiving which a natural scientist has about sociological observations is that it is difficult to make them as independent of the observer as physical observations can be. What do Halsey and Trow themselves think about elitism versus expansion? And do their views bias their observations? This the reader must be left to decide for himself. Though detecting glimpses of the authors' opinion, I am satisfied that they have achieved a remarkable objectivity.

As for style, there is none of the exasperating jargon (commoner, it is true, from America than from Britain) behind which lesser sociologists conceal the ambiguity of their thoughts. The style is courageously simple and clear. It displays, for posterity, the state of the British academic profession at a critical point in its history. ERIC ASHBY

Heartfelt Tale

The History of Coronary Heart Disease. (New Series: Vol. xviii.) By J. O. Lebowitz. Pp. xvii+227+15. (Wellcome Institute: London, December 1970.) £3.

CORONARY heart disease is an indiscriminate killer that strikes men down in their prime. In the present century it is one of the scourges of modern life, having replaced smallpox and other infectious diseases as a major hazard to mankind. In medicine, as in other fields of human activity, knowledge of history makes the present more comprehensible even if the future remains unpredictable and, with this in mind, Dr J. O. Lebowitz has written a history of coronary heart disease.

His book provides an excellent background to understanding the present state of medical knowledge in this field. Starting with antiquity and the Middle Ages, he traces the first tentative glimmerings of knowledge of early writers who were concerned on the one hand to define the anatomy and function of the coronary circulation, and on the other to describe individual clinical problems causing sudden death. In the seventeenth century, William Harvey's discovery of the circulation of the blood provided the major physiological break-

through on which all subsequent development was based. During the next hundred years, an increasing number of clinical reports of individual cases was published and Dr Leibowitz draws attention to a well documented account of rupture of the heart described by Harvey himself in 1649. But it was not until the eighteenth century that advances in clinical medicine and pathology began to parallel those which had taken place earlier in the basic sciences, and Heberden's classical description of angina pectoris, never bettered by any writer since, was published in 1769. Within ten years disease of the coronary arteries was recognized as causing angina pectoris and by the end of the century the work of Parry, Jenner and others had clearly established the relationship between coronary artery disease, angina pectoris and sudden death. The nineteenth century saw the development of cellular and vascular pathology, but only in the twentieth century, with the advent of electrocardiography, was coronary heart disease in its manifold forms fully recognized and Dr Leibowitz unfolds a fascinating story of the developments which have taken place during the past fifty years. Investigation at present is directed specifically to the study of aetiology and prevention, and the book concludes with an up to date account of contemporary thought.

This book is a work of scholarship drawing on the widest possible range of sources and providing an excellent bibliography. Footnotes are well written and unobtrusive, yet provide useful small print information. There is an unexpected error in the identity of a Dr Anonymous who had left his body to Dr Heberden for dissection following his death from angina pectoris in 1772. The autopsy failed to show any abnormality of the heart. Dr Leibowitz identified this public spirited patient as Dr Haygarth of Chester, a physician of outstanding repute in the field of infectious fevers. Haygarth, however, cannot have been Heberden's patient, for he lived on until 1827 when he died in Bath at the advanced age of 87. Such minor points do not detract in any way from the excellence of this scholarly account of one of the major diseases of modern times.

C. C. BOOTH

Catching the Light

Invertebrate Photoreceptors: a Comparative Analysis. By Jerome J. Wolken. Pp. xi+179. (Academic: New York and London, May 1971.) \$9.50; £4.45.

IN spite of a generalized title, J. J. Wolken's little book is an illustrative rather than an exhaustive comparative study of invertebrate photoreceptors.

By way of introduction the book begins with a description of the electromagnetic spectrum and the physics of light, and this is combined with equally useful information concerning the classification and basic biochemistry of the photosensitive pigments found in plants and animals.

The comparative section begins with that group of animals which has been neglected perhaps the most by photobiologists—the Protozoa—illustrated in this case by the flagellate, *Euglena gracilis*. The fine structures of the flagellum and eyespot are described and experimental details of the animals' photobehaviour are integrated with microspectrophotometric studies of the various organs involved. This is followed by a consideration of the compound eye as found in many insects and Crustacea. Some nine genera of arthropods are described in detail, including the copepod *Copilia*, a species which has become ubiquitous in textbooks of late, presumably because of the perversely unusual visual apparatus it possesses. The invertebrate survey is concluded with a study of the structure of the photoreceptors found in the refracting eye of cephalopod molluscs, such as the squid. It was wise of the author to contrast all the invertebrate structures with the vertebrate retinal rod. The whole forms a good introduction to the study of photoreceptor structure and the subject is made all the more easy to grasp by virtue of the many fine micrographs which form the text figures.

The second part of the book is concerned with the vertebrate and invertebrate visual pigments and deals with techniques for their extraction and purification. The various absorption spectra as measured both *in vitro* and *in vivo* are then presented and discussed, as are similar results for the accessory and screening pigments found in association with the various photoreceptors.

An important generalization in the concluding section is that a functional difference exists between the "open" type of rhabdomere arrangement found in the dipterous insects and the "closed" or fused rhabdomeres of many insects and Crustacea (excepting, of course, *Copilia* which is of the open type). This difference is seen as the adaptation of the closed type to vision at low light intensities, which is fair enough except to say that many insects with closed type rhabdomeres, for example, the bees and wasps, the dragonflies and perhaps the locusts and grasshoppers, are as diurnal in habit as any of the open eyed Diptera. To correlate the structural findings with the electrophysiological evidence the author associates the open eye with the "fast" category of electroretinogram and the closed eye with the "slow" type. Once again the bees are usually considered as having the

fast electrical responses, yet are shown to possess the closed rhabdomere arrangement, so that one feels the author should have presented a rather fuller argument for his interpretation of photoreceptor fine structure.

Omitting as it does almost all reference to the electrophysiological events associated with visual excitation, this book leaves the impression of a story unfinished, and this is one reason why *Invertebrate Photoreceptors* remains a good basis for the study of the subject but lacks the breadth to make it a thoroughgoing comparative account.

JOHN PATTERSON

Snakes of Two Regions

A Field Guide to the Snakes of Southern Africa. By V. F. M. Fitz-Simons. Pp. 221+12 plates. (Collins: London, January 1971.) £2.10.

The Snakes of Europe. By J. W. Steward. Pp. 238+28 photographs. (David and Charles: Newton Abbot, March 1971.) £2.75.

EUROPE has thirty-three species of snakes, only five of them confined to the area. There was a general work on European reptiles nearly a hundred years ago and a book devoted to the snakes in particular nearly sixty years ago. Mr Steward brings us up to date on the basis of years of field and vivarium experience and much travel. Southern Africa has three and a half times the number of species, about forty-two of them endemic, and may well have undiscovered forms. Dr FitzSimons's handbook is based on his own pioneering studies in the museum and the field.

Both works recognize a considerable number of subspecies. Although both authors sometimes pause to express doubts about the status of some taxa neither of them discusses the nature of subspecies and makes it clear that they are subjective categories; the existence of zones of intermediacy is barely hinted. Surely the non-specialist would have been better served by an informal survey of the variant regional populations, some of which have been recognized as subspecies. I make this comment partly because I believe that, in many cases, when a larger number of characters is studied, many of them will be found to vary independently and many of the subspecies boundaries be seen to be arbitrary.

Both authors give aids to identification but neither takes the reader gently by the hand through the problems nor mentions museums as a source of information. FitzSimons groups most, but not all, of the snakes by predominant colour and pattern. If one's snake be mostly brown, however, there are fifty-nine to choose from; this can be narrowed further if it be banded,

spotted, striped or plain, but a considerable choice would still remain. Steward has a dichotomous key based on simple characters but some of these, for example scale-row counts, are not explained in text or figures. So, in either case, to be reasonably sure, the novice might often finish up scanning the generous illustrations (many in colour for Southern Africa) and wading through individual accounts.

FitzSimons gives a tabular summary of distributions by regions. He gives English and Afrikaans names but only occasionally notices that the snakes have African names. A valuable feature of Steward's book is a distribution map for every species and subspecies. My only comment is that the firmness of the boundary lines can be misleading and is sometimes at variance with the text. There are outline figures of the head scales of most species, unfortunately rather small in relation to the size of the page, and some of them rather vague; several have no nostril. Another valuable feature is a list of the common names in thirteen European languages.

The great value of both of these works lies in the precise description of each form with an account of the habits, where they are known. Sometimes I pause to wonder just how many years of field experience have gone into just a couple of sentences. The books are of about the same size. FitzSimons's work understandably gives more space to snakebite. Perhaps because the European snake fauna is smaller, Steward has more room to discuss the habits of snakes, to interpret their distribution patterns and to convey his personal enthusiasm.

I wish both these works many years of useful service and further editions.

GARTH UNDERWOOD

Hodograph Equations

The Hodograph Equations: an Introduction to the Mathematical Theory of Plane Transonic Flow. By A. R. Manwell. (University Mathematical Monographs.) Pp. ix+476. (Oliver and Boyd: Edinburgh, February 1971.) £10.

ALTHOUGH this book has the title *The Hodograph Equations* it is almost exclusively concerned with the application of the hodograph method to the problem of the plane transonic flow of an inviscid gas. This approach to gas dynamics was pioneered at the beginning of this century by Chaplygin and received a tremendous impetus after the end of the Second World War as the study of transonic phenomena was intensified. The author gives a detailed account of the work up to about 1965. Although slanted to some extent towards the interests of his own consider-

able contributions to the subject over some twenty years, a very fair overall picture of the subject is presented and the work of the leading research workers such as Tricomi, Lighthill, Guderley, Frankl, Germain and Morawetz, is described in considerable detail. The list of references is not intended to be complete but is highly representative of the major contributions.

The book professes to be aimed at honours graduates in mathematics and engineering, and presupposes a relatively modest knowledge of fluid dynamics and a somewhat more exacting one of classical analysis, although where practicable the author attempts to provide the necessary mathematical background. This leads to lengthy sections on partial differential equations, integral equations and special functions, and accounts in part for the formidable size of the book. Indeed the whole approach is geared primarily to the mathematician, and this is reflected in the preface where it is stated that "the arrangement of the various items is as far as possible in the order of their analytical complexity". This seems a strange principle to adopt as a criterion for ordering and as a result the reader is left with an uneasy impression of having jumped about from one topic to another. With a subject of this nature—relatively narrow from the physicist's standpoint but giving scope for enormous mathematical complexity—the author has a difficult task in that he wishes to present a book which is self-contained and does not require the reader to make constant reference to research papers or other textbooks. At the same time the serious student of the subject may regret the lack of a more extensive bibliography. Professor Manwell writes with the authority of one who has read the literature widely and deeply, and would, one feels, be in a position to supply detailed references, amplified where necessary with expert comment.

Unfortunately, the general impression which the printed format of the book gives is not favourable. The intricate nature of the mathematics calls, perhaps understandably, for the introduction of a plethora of asterisks, bars, tildes, subscripts and superscripts together with a vast range of basic symbols, and there is ample evidence that at times these demands have over-extended the resources of the compositor. Moreover, there are numerous proof reading errors and a complete lack of consistency in the use of symbols, brackets and spaces. A particularly unhappy example is the way in which throughout the entire text a full stop is introduced in a random manner into the middle of mathematical expressions to indicate multiplication. (Equation (14.3) and the line above it illustrate the lack of any consistent pattern.) Other examples are the indis-

criminate use of two different founts for the superscript ξ on numerous occasions from p. 59 on, and the fact that the o, O order symbols are sometimes put in italics and sometimes not. Factual errors also occur. For example, in (19.36), $\psi_{(c)}$ does not satisfy Laplace's equation as is required; its compressible analogue in (19.37) is also wrong, and is not even the correct equivalent form of the incorrect version of (19.36). In spite of the inherent interest of much of the material the book is marred by faulty proof reading, poor display of mathematical expressions and indifferent diagrams, and seems overpriced at £10.

A. G. MACKIE

Ancient Astronomy

Ancient Astronomical Observations and the Accelerations of the Earth and Moon. By Robert R. Newton. Pp. xviii + 309. (Johns Hopkins: Baltimore, Maryland, and London, December 1970.) £4.75.

IN 1853 J. C. Adams pointed out that the then theoretical value of the gravitational secular acceleration of the Moon's mean motion, which agreed reasonably well with observation, was erroneous and should be reduced to little more than half. The original value stemmed from the combination of the historic discovery by Laplace in 1787 that the secular acceleration was due to the slow diminution in the eccentricity of the Earth's orbit and of a demonstrable error in the analytical derivation (the variable eccentricity had been treated as a constant during the integration of the differential equation). The resulting discordance with observation led to immense activity both in the verification and improvement of the theory, and in the critical examination of the observations.

The discordance could not be resolved since it was due to two distinct but related non-gravitational causes: the variable speed of the rotation of the Earth, giving rise to non-uniformity in the time-scale of mean solar time; the dissipation of energy, and the transfer of angular momentum within the Sun-Earth-Moon system, chiefly due to tidal friction.

In 1939 the Astronomer Royal, H. Spencer Jones, summarized all available data from modern (after 1680) observations of the Sun, Moon and planets and combined these with the results obtained by J. K. Fotheringham from ancient observations. He demonstrated conclusively the reflexion of the Earth's irregular rotation in the motions of the Sun, Moon and planets and determined the so called secular accelerations of the Sun and Moon. The results were subsequently used to define the time-scale

of ephemeris time and the adopted secular acceleration of -22.44^{11} (century) $^{-2}$ in the Moon's mean longitude.

In his book R. R. Newton rediscusses the ancient observations and comes to the conclusion (in the opposite sense to Adams) that they support an average value of almost double the currently adopted value. There can be no question either of the importance and value of Newton's contribution or of the impetus that it will give (and, since preprints were widely circulated in September 1968, has given) to research in this field, particularly the analysis of both ancient and modern observations.

The basic unresolved problem is geophysical in respect of the medium term behaviour of the Sun-Moon-Earth system: can the dissipative effects have changed by a factor of 2 in the past 2,000 years, or are either the ancient or modern observations (or analyses, or both) suspect? The question throws doubt on the efficacy of the determination of ephemeris time from observations of the Moon in indicating possible cosmological differences from atomic time. Newton only touches this matter lightly in his final chapter, being otherwise content to present the evidence.

The main part of the book is devoted to a detailed investigation into the records of ancient eclipses and their interpretation. This is a specialist field, much aided now by precise predictions, but involving scholarship of high order and judgment; Newton is very critical of the methods of his predecessors who, in his view, tended to introduce bias by forcing identification. Not all will agree with his interpretations, however; and his methods of analysis are not always as precise as might be desired. But he provides very full information of his sources, his arguments and his treatment; he reviews critically most modern investigations, and he gives a valuable digest of the many confusing notations that have been used. It is a quite invaluable contribution and one that no research worker in either the astronomical or geophysical fields concerned can afford not to have.

D. H. SADLER

Peculiar Stars

Stellar Spectroscopy: Peculiar Stars. By Margherita Hack and Otto Struve. Pp. 317. (Observatorio Astronomico di Trieste: Trieste, 1970.)

THIS book is the second part of the updated revision of a text originally written about ten years ago but not published at the time because of Otto Struve's death in 1963, and it fills a substantial gap by providing a detailed survey of the results of stellar spectroscopy from a chiefly observational point

of view. Normal stars were dealt with in the first part of the series.

The concept of peculiar stars is relative: some unusual stars are merely extreme cases of processes in stellar evolution or stellar atmospheres that are believed to be fairly well understood, while other groups of quite frequent occurrence are more or less baffling in the present state of knowledge. Furthermore, it is convenient to group together stars of widely differing evolutionary status having common characteristics such as emission lines. This book accordingly concentrates on three broad classes: hot stars with emission lines; novae and other explosive variables (which also have emission lines); and magnetic, metallic-line and related stars. Other groups like T Tauri and symbiotic stars are mentioned only in passing. The text is partly expository and partly composed of skilfully blended quotations from review articles.

The task of providing a coherent survey of these diverse and only partially understood types of stellar spectrum is difficult, and Mrs Hack has done remarkably well in making the material coherent and reasonably up to date. There are gaps: for example, the possibility of collisional excitation in nova spectra has been ignored and there is no reference to the important work done on non-dipolar fields in magnetic stars. Also some of the arguments used do not have a clear physical basis, particularly on the rather fiendish problems involved in interpreting the behaviour of magnetic spectrum variables. However, the book is a good summary of the observational data in its chosen fields and will provide an excellent starting point for students embarking on an investigation of peculiar stars. BERNARD PAGEL

Chemical Texts

Physical Methods of Chemistry. Edited by Arnold Weissberger and Bryant W. Rossiter. Part 1A: *Components of Scientific Instruments.* Pp. xi+433. £9.50. Part 1B: *Automatic Recording and Control, Computers in Chemical Research.* Pp. 330. £8. (Techniques of Chemistry, Vol. 1.) (Wiley-Interscience: New York and London, May 1971.)

"TECHNIQUES of Chemistry" is the replacement for the well-known series "Techniques of Organic Chemistry" and the first volume, *Physical Methods of Chemistry*, succeeds *Physical Methods of Organic Chemistry*. Part 1A, *Components of Scientific Instruments*, contains chapters on mechanical and electronic components, the latter being preceded by a chapter on basic electrical principles. Finally, there is a chapter on the generation and modulation of

waves (both electromagnetic and acoustic).

The standard of presentation is variable, and in some cases the rate of progress from an elementary start to more sophisticated matter is alarming. Thus, much of the material must appear to be either far too elementary or too difficult for any particular reader. This volume is therefore unlikely to be attractive to individuals and will only find a ready sale to libraries. Even here it would seem that, for a good proportion of the material, likely users will find other specialized texts (not necessarily more advanced) more valuable. It is particularly irritating to find, in a volume as expensive as this, much wasted space. While this is clearly a personal view, I find it difficult to believe that pages of photographs devoted to "view of typical printed circuit card, card rack, hand-wired circuit board, typical multi contact connectors", and such like, can be justified.

Part 1B, *Automatic Recording and Control, Computers in Chemical Research*, contains four chapters. The first, on detection, is principally concerned with various transducers for converting in most instances a change in a particular physical property into an electrical signal, and related matters. I found this chapter interesting and believe that it could be helpful to many. The next very short chapter on automatic recording reads like a collection of technical specifications for various recorders. Such information is freely available, indeed it is difficult to avoid receiving much of it, from manufacturers.

The third chapter, on automatic control, discusses linear feedback control networks, the ways of obtaining data and applications of basic principles to specific systems and the use of feedback for some typical controllers used in chemical apparatus. For those concerned with designing apparatus for chemical research this chapter could be valuable and should enable them to talk sensibly with their senior electronics technicians. The title of the final and longest chapter, "Computers in Chemical Research", is misleading: nearly sixty pages are devoted to Fortran. Surely nobody wishing to learn this language will turn to a book of this type. Similarly, although they make quite easy reading, the history, basic principles and a long and elementary discussion of binary arithmetic and Boolean algebra are out of place in a book about techniques of chemistry. Part of the relatively small fraction of this chapter on digital computers has some real value in the context of this volume. I can imagine very few individuals buying this volume, for more than half of the material is readily available elsewhere at considerably lower cost.

H. M. FREY

CORRESPONDENCE

Science and Development

SIR,—I wish that your discussion of the relevance of science in developing countries (*Nature*, 232, 73; 1971) could have started some 25 years ago when, after centuries of foreign rule, most of the countries under the old British Empire were beginning to emerge as free nations. It could probably then have saved some of the new governments of those countries from taking decisions which have led to serious economic and social problems. The crying need of millions of people in these countries is for food and shelter and if science and technology has any relevance to humanity then it should be the foremost aim to provide these basic necessities as soon as possible. Development of agriculture and the related industry must therefore be the first task. In order to develop agriculture the research must be oriented to develop better strains of wheat, rice, etc., on one hand and "intermediate" tools of agriculture on the other hand. (What I mean by "intermediate" tools is the sort of tools which are in between the primitive plough drawn by the horse or bullock and the complex tractor.) The intermediate tools would have the advantage that they could be more efficient than the primitive tools used at present and be mechanically simple to be looked after by the simple farmer himself.

Communication to the men in the villages of these countries (and about 80% of the population in a country like India lives in villages) is another equally, if not the most, important aspect to which very little attention has been paid with the result that whatever developments were

made in these fields remained confined to reports in the files of government officials.

Without the communication of these new developments to the farmers in the villages, no real progress on the farms can be achieved since it is the farmers in the villages and not the officials who work on the farm. I believe that it is here that the medium of television could provide the means to communicate to the farmer, in his own language, the new developments in tilling the soil, sowing, fertilizers, maintenance of his tools, etc., since any written material, such as books, is no good to him because he cannot read. Even illiteracy could be effectively tackled by the programmes on the television specially designed for this purpose. Italy is known to have achieved, during the last decade, a great success in its agriculture and literacy programme by use of television. I am sure the same can be done in the case of developing nations. Here is a place for the advanced technology in the economics and social advancement of slowly advancing countries.

Education of the illiterate masses through television, I am sure, will make a great impact on the quality of life to millions of people and bring about an awareness of the world around them. As such, at present they are in complete darkness about the better way of life existing a few miles away in their own land, not to mention foreign lands. Television could be used to teach them simple ways and means to improve their own lot and their children's future in the circumstances in which they find themselves. I can visualize the application of television to convince the people

of the need to control the population explosion, to improve their sanitary conditions, how to avoid malnutrition with available food. Without the use of this medium, I am afraid, the progress in developing countries will take too long, which would have a disastrous effect the world over. The cost of providing a network of television stations throughout these countries would be well worth the improvements in the lives of millions of people and would be repaid by the increase in production on the farms.

Organized research on an international scale, as you mention, of problems such as health, cheap housing, etc., can easily contribute towards the development of the developing countries. But what is foremost is the need for the realization by the leaders of these nations to orient, in the interest of the people they serve, their policies so as to attract capital from inside and outside the countries in order to enable them to exploit the technology which already exists or is developed by their own efforts for the solution of these problems. This would not only generate the growth of their economies but at the same time enable them gainfully to employ their trained manpower, since unemployment and under-employment of the vast number of the school leavers and graduates lead to serious social problems and no democracy can survive and grow with the existing social conditions of extreme poverty and misery.

Yours faithfully,

K. C. TRIPATHI

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Obituary

Sir W. Le Gros Clark

WHEN Wilfrid Le Gros Clark went to Oxford in 1934 (after holding chairs at St Bartholomew's and St Thomas's Hospitals) to become Dr Lee's professor of anatomy at the age of 39, he was already the acknowledged master and leader in three exciting and expanding fields. Largely through the example of his own meticulous and imaginative investigations of the visual and olfactory pathways and of the connexions of the thalamus, descriptive neuroanatomy had begun to make way for much more significant enquiries into cerebral functional organization. The basis of Le

Gros Clark's success in this field was laid by his researches into the comparative neurology of lower primates, particularly of tarsier and tree shrews, specimens of which he obtained during his time as principal medical officer in Sarawak (1920–23). This in turn led him deeply into primate and human evolution; his pre-eminence in this field was marked by the publication in 1934 of his influential *Early Forerunners of Man*, later revised in several editions as *The Antecedents of Man* (1959).

His creative and original approaches to neurology, morphology and phylogeny

led him on to his reforming activities in both teaching and research in human anatomy and physical anthropology. In anatomy he insisted on experimentation to reveal the functional significance of structure as the way forward. His *Tissues of the Body*, now in its fifth edition, must have reconciled many a medical student to the load placed on him by an over-traditional subject. And he strove for the introduction of shorter textbooks, more in keeping with a modern curriculum, bringing out his own *Practical Anatomy* (1948) and later contributing to the *Text Book of Human*



Anatomy (edited by W. J. Hamilton). Likewise, in physical anthropology, an old-established subject in Oxford, Le Gros Clark firmly opposed the traditional fare of craniometry and typology, advocating instead a genuine study of human variation in relation to both environmental and genetic factors.

All these issues were fostered by him in Oxford over the next 25 years. His vision and integrity, his positive outlook, his critical and creative power, his erudition, his unfailing kindness, as well as the example of his own sustained productivity, made him an impressive and inspiring head of a large and many sided department. A stream of visitors and postgraduate students came to the department to work with, under, or just near 'Le Gros'.

In the war years a team under his lead demonstrated a new facet of functional anatomy by designing equipment to meet the visual, auditory, manipulative and postural requirements of Service personnel such as gunners performing complex tests of sighting and tracking.

This experience of "human engineering" or ergonomics convinced Le Gros Clark of its value for everyday activities, particularly in industry. An MRC unit, attached to his department and of which he was honorary director (1948–1962), pursued a programme devoted largely to practical applications of functional anatomy, human physiology and physical anthropology.

In the last decade of his tenure at Oxford, Le Gros Clark continued his neurological work but became more and more immersed in his palaeontological interests. On a visit to South Africa he was able to study at first hand the australopithecine material, accumulated by Raymond Dart and Robert Broom. He became entirely convinced of the hominid status of these creatures, though he remained sceptical of the proved existence of a form as advanced as *Homo habilis*. He also carried out the definitive descriptions of the pre-hominid material (notably Proconsul) discovered by Louis Leakey. In all this he was never a mere taxonomist, but strove always to define the phylogenetic processes at work. His conclusions on the course of primate and human evolution are set out succinctly in three notable books, *History of the Primates* (8th edition, 1967), *The Fossil Evidence for Human Evolution* (1955), and *Man Apes or Ape Men?* (1967). Le Gros Clark also contributed significantly to the solution of the long standing Piltdown problem (1953).

Somewhat to his surprise Le Gros Clark encountered not inconsiderable opposition both to his reforming activities and to his views on fossil man. Polemics he found distasteful and distressing, but he was a formidable protagonist in controversy, deriving his strength from the painstaking and concentrated consideration and reconsideration he gave to everything he studied.

In some ways Le Gros Clark was a man of paradox. While he went to considerable trouble to discourage the

study of anatomical minutiae, he himself retained an awesome knowledge of the detailed macro and micro-anatomy of the human frame and indeed delighted in the art of topographical disquisition. He heartily disliked administration, the role of "organization man" or "scientist-politician" was not to his taste; yet he directed his large department unobtrusively and with efficiency, paying careful attention to its rebuilding, expansion and modernization. He remained a firm believer in simple apparatus and simple experimentation, and often expressed scepticism of the need for expensive equipment, even of the electron microscope; nevertheless when fully convinced, he would spare no trouble to see that the necessary equipment was obtained. For a generation Le Gros Clark was the outstanding British anatomist and its leader, yet he strove always to keep aloof from scientific politics, though in a few crises when he felt impelled to intervene his influence was decisive.

Le Gros Clark was elected to the Royal Society in 1935 and awarded a Royal Medal in 1961. He was president of the International Anatomical Congress at Oxford in 1950, president of the Anatomical Society in 1952 and 1953 and president of the British Association in 1961. He also served on the Medical Research Council. He was a member and master (1954) of the Salters Company and fellow of Hertford College, Oxford. He was knighted in 1955 and retired in 1962. He published a volume of memoirs, *Chant of Pleasant Exploration*, in 1968.

In 1923 he married Freda Constance Giddey, by whom he had two daughters. Freda Le Gros Clark died in 1963. In 1964 he married Violet, widow of Dr Leonard Browne.

The combination of Wilfrid Le Gros Clark's gifts and the diversity of his interests has without doubt made a long-lasting impression on the content and style of British anatomy and allied disciplines.

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